CLAIMS

We claim:

1. An ICE inhibitor comprising:

(a) a first and a second hydrogen bonding moiety, each of said moieties being capable of forming a hydrogen bond with a different backbone atom of ICE, said backbone atom being selected from the group consisting of the carbonyl oxygen of Arg-341, the amide -NH- group of Arg-341, the carbonyl oxygen of Ser-339 and the amide -NH- group of Ser-339;

(b) a first and a second moderately hydrophobic moiety, said moieties each being capable of associating with a separate binding pocket of ICE when the inhibitor is bound thereto, said binding pocket being selected from the group consisting of the P2 binding pocket, the P3 binding pocket, the P4 binding pocket and the P' binding pocket; and

(c) an electronegative moiety comprising one or more electronegative atoms, said atoms being attached to the same atom or to adjacent atoms in the moiety and said moiety being capable of forming one or more hydrogen bonds or salt bridges with residues in the P1 binding pocket of ICE.

2. The ICE inhibitor according to claim 1, wherein said inhibitor is characterized by a neutral or favorable enthalpic contribution from the sum of all electrostatic interactions between the inhibitor and ICE when the inhibitor is bound thereto.

3. The ICE inhibitor according to claim 1, wherein said inhibitor has a molecular weight less than or equal to about 700 Daltons.

4. The ICE inhibitor according to claim 3, wherein said inhibitor has a molecular weight between about 400 and about 600 Daltons.

5. The ICE inhibitor according to claim 1, wherein said inhibitor further comprises less than two secondary amide bonds.

6. The ICE inhibitor according to claim 1, wherein said inhibitor further comprises less than two groups selected from the set consisting of secondary amide groups and carbamate groups.

7. The ICE inhibitor according to claim 1, wherein said inhibitor further comprises a polysubstituted cyclic group having between three and seven substituents, said cyclic group not comprising the first or second moderately hydrophobic moiety or the electronegative moiety.

8. The ICE inhibitor according to claim 1 or 7, wherein said inhibitor is characterized by a strain energy of binding of said inhibitor to ICE less than or equal to about 10 kcal/mole.

9. The ICE inhibitor according to claim 1 or 7, wherein when said inhibitor is bound to ICE at least two of the following four conditions 1) through 4) are met:

1) one of said moderately hydrophobic moieties associates with the P2 binding pocket of ICE, in such a way that:

a) the distance from the center of mass of the moderately hydrophobic moiety in the P2

binding pocket to the carbonyl oxygen of Arg-341 of ICE is between about 7.1Å and about 12.5Å;

b) the distance from the center of mass of the moderately hydrophobic moiety in the P2 binding pocket to the amide nitrogen of Arg-341 of ICE is between about 6.0Å and about 12Å; and

c) the distance from the center of mass of the moderately hydrophobic moiety in the P2 binding pocket to the carbonyl oxygen of Ser-339 of ICE is between about 3.7Å and about 9.5Å;

2) one of said moderately hydrophobic moieties associates with the P3 binding pocket of ICE in such a way that:

a) the distance from the center of mass of the moderately hydrophobic moiety in the P3 binding pocket to the carbonyl oxygen of Arg-341 of ICE is between about 3.9Å and about 9.5Å;

b) the distance from the center of mass of the moderately hydrophobic moiety in the P3 binding pocket to the amide nitrogen of Arg-341 of ICE is between about 5.4Å and about 11Å; and

c) the distance from the center of mass of the moderately hydrophobic moiety in the P3 binding pocket to the carbonyl oxygen of Ser-339 of ICE is between about 7.0Å and about 13Å;

3) one of said moderately hydrophobic moieties associates with the P4 binding pocket of ICE in such a way that:

a) the distance from the center of mass of the moderately hydrophobic moiety in the P4 binding pocket to the carbonyl oxygen of Arg-341 of ICE is between about 4.5Å and about 7.5Å;

b) the distance from the center of mass of the moderately hydrophobic moiety in the P4

binding pocket to the amide nitrogen of Arg-341 of ICE is between about 5.5Å and about 8.5Å; and

c) the distance from the center of mass of the moderately hydrophobic moiety in the P4 binding pocket to the carbonyl oxygen of Ser-339 of ICE is between about 8Å and about 11Å; and

4) one of said moderately hydrophobic moieties associates with the P' binding pocket of ICE in such a way that:

a) the distance from the center of mass of the moderately hydrophobic moiety in the P' binding pocket to the carbonyl oxygen of Arg-341 of ICE is between about 11Å and about 16Å;

b) the distance from the center of mass of the moderately hydrophobic moiety in the P' binding pocket to the amide nitrogen of Arg-341 of ICE is between about 10Å and about 15Å; and

c) the distance from the center of mass of the moderately hydrophobic moiety in the P' binding pocket to the carbonyl oxygen of Ser-339 of ICE is between about 8Å and about 12Å.

10. The ICE inhibitor according to claim 1 or 7, wherein when said inhibitor is bound to ICE, said moderately hydrophobic moieties separately associate with the P' binding pocket of ICE and the P2 binding pocket of ICE and the distance from the center of mass of the moderately hydrophobic moiety in the P' binding pocket to the center of mass of the moderately hydrophobic moiety in the P2 binding pocket is between about 6.5Å and about 13Å.

11. The ICE inhibitor according to claim 1 or 7, wherein when said inhibitor is bound to ICE,

said moderately hydrophobic moieties separately associate with the P' binding pocket of ICE and the P3 binding pocket of ICE and the distance from the center of mass of the moderately hydrophobic moiety in the P' binding pocket to the center of mass of the moderately hydrophobic moiety in the P3 binding pocket is between about 6Å and about 15Å.

12. The ICE inhibitor according to claim 1 or 7, wherein when said inhibitor is bound to ICE, said moderately hydrophobic moieties separately associate with the P' binding pocket of ICE and the P4 binding pocket of ICE and the distance from the center of mass of the moderately hydrophobic moiety in the P' binding pocket to the center of mass of the moderately hydrophobic moiety in the P4 binding pocket is between about 14Å and about 22Å.

13. The ICE inhibitor according to claim 1 or 7, wherein when said inhibitor is bound to ICE, said moderately hydrophobic moieties separately associate with the P2 binding pocket of ICE and the P3 binding pocket of ICE and the distance from the center of mass of the moderately hydrophobic moiety in the P2 binding pocket to the center of mass of the moderately hydrophobic moiety in the P3 binding pocket is between about 5.5Å and about 13Å.

14. The ICE inhibitor according to claim 1 or 7, wherein when said inhibitor is bound to ICE, said moderately hydrophobic moieties separately associate with the P2 binding pocket of ICE and the P4 binding pocket of ICE and the distance from the center of mass of the moderately hydrophobic moiety

in the P2 binding pocket to the center of mass of the moderately hydrophobic moiety in the P4 binding pocket is between about 9Å and about 17Å.

15. The ICE inhibitor according to claim 1 or 7, wherein when said inhibitor is bound to ICE, said moderately hydrophobic moieties separately associate with the P3 binding pocket of ICE and the P4 binding pocket of ICE and the distance from the center of mass of the moderately hydrophobic moiety in the P3 binding pocket to the center of mass of the moderately hydrophobic moiety in the P4 binding pocket is between about 7.5Å and about 17Å.

16. The ICE inhibitor according to claim 1 or 7, wherein when said inhibitor is bound to ICE, said first hydrogen bonding moiety forms a hydrogen bond with the carbonyl oxygen of Ser-339 of ICE and said second hydrogen bonding moiety forms a hydrogen bond with the carbonyl oxygen of Arg-341 of ICE and wherein the distance between said hydrogen bonding moieties is between about 5Å and about 7.5Å.

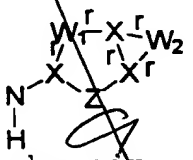
17. The ICE inhibitor according to claim 1 or 7, wherein when said inhibitor is bound to ICE, said first hydrogen bonding moiety forms a hydrogen bond with the carbonyl oxygen of Ser-339 of ICE and said second hydrogen bonding moiety forms a hydrogen bond with the amide -NH- group of Arg-341 of ICE and wherein the distance between said moieties is between about 2.5Å and about 5Å.

18. The ICE inhibitor according to claim 1 or 7, wherein when said inhibitor is bound to ICE,

said first hydrogen bonding moiety forms a hydrogen bond with the carbonyl oxygen of Arg-341 of ICE and said second hydrogen bonding moiety forms a hydrogen bond with the amide -NH- group of Arg-341 of ICE and wherein the distance between said hydrogen bonding moieties is between about 2.5Å and about 4Å.

19. An ICE inhibitor comprising:

(a) a scaffold of formula I:

(I) 

wherein:

each X is independently C or N;

Z is CO or SO_2;

W_1 is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different X atoms through bonds r;

W_2 is a straight chain comprising 3-5 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different X atoms through bonds r;

each bond labeled r is independently a single or a double bond;

H is a first hydrogen bonding moiety and Z is a second hydrogen bonding moiety, each of said moieties being capable of forming a hydrogen

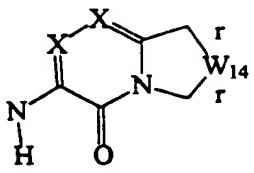
bond with a different backbone atom of ICE, said backbone atom being selected from the group consisting of the carbonyl oxygen of Arg-341, the amide -NH- group of Arg-341, the carbonyl oxygen of Ser-339 and the amide -NH- group of Ser-339;

(b) a first and a second moderately hydrophobic moiety, said moieties each being covalently bound to said scaffold and each being capable of associating with a separate binding pocket of ICE when the inhibitor is bound thereto, said binding pocket being selected from the group consisting of the P2 binding pocket, the P3 binding pocket, the P4 binding pocket and the P' binding pocket; and

(c) an electronegative moiety comprising one or more electronegative atoms, said atoms being attached to the same atom or to adjacent atoms in the moiety and said moiety being covalently bound to said scaffold and being capable of forming one or more hydrogen bonds or salt bridges with residues in the P1 binding pocket of ICE.

20. The ICE inhibitor according to claim 19, wherein said scaffold has the formula:

(IA)



wherein:

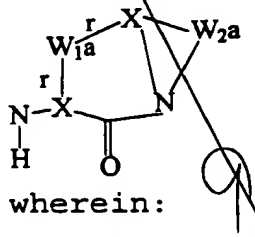
each X is independently C or N;

W_{14} is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or

unsaturated and said chain comprising two ends which are covalently bound to two different C atoms through bonds r; and

each bond labeled r is independently a single or a double bond.

21. The ICE inhibitor according to claim 19, wherein said scaffold has the formula:

(IB) 

wherein:

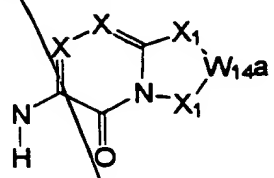
X is C or N;

W_{1a} is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different X atoms through bonds r;

W_{2a} is a straight chain comprising 3-4 covalently bound members independently selected from the group consisting of C, N, S and O, said chain comprising two ends which are covalently bound to two different atoms to form an aryl or heteroaromatic ring therewith; and

each bond labeled r is independently a single or a double bond.

22. The ICE inhibitor according to claim 19, wherein said scaffold has the formula:

(IC) 

wherein:

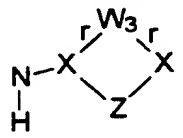
each X is independently C or N;

each X_1 is independently C, N, or O; and

W_{14a} is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being saturated or unsaturated and said chain comprising two ends which are covalently bound to two different X_1 atoms to form a non-aromatic ring therewith.

23. An ICE inhibitor comprising:

a scaffold of formula II:

(II) 

wherein:

each X is independently C or N;

Z is CO or SO_2;

W_3 is a straight chain comprising 2-4 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different X atoms through bonds r;

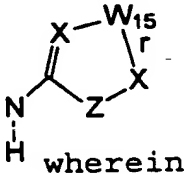
each bond labeled r is independently a single or a double bond;

H is a first hydrogen bonding moiety and Z is a second hydrogen bonding moiety, each of said moieties being capable of forming a hydrogen bond with a different backbone atom of ICE, said backbone atom being selected from the group consisting of the carbonyl oxygen of Arg-341, the amide -NH- group of Arg-341, the carbonyl oxygen of Ser-339 and the amide -NH- group of Ser-339;

(a) a first and a second moderately hydrophobic moiety, said moieties each being covalently bound to said scaffold and each being capable of associating with a separate binding pocket of ICE when the inhibitor is bound thereto, said binding pocket being selected from the group consisting of the P2 binding pocket, the P3 binding pocket, the P4 binding pocket and the P' binding pocket; and

(b) an electronegative moiety comprising one or more electronegative atoms, said atoms being attached to the same atom or to adjacent atoms in the moiety and said moiety being covalently bound to said scaffold and being capable of forming one or more hydrogen bonds or salt bridges with residues in the P1 binding pocket of ICE.

24. The ICE inhibitor according to claim 23, wherein said scaffold has the formula:

(IIA) 

wherein:

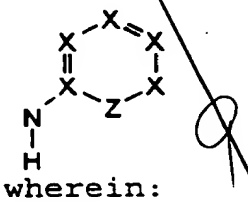
each X is independently C or N;

Z is CO or SO_2;

W_{15} is a straight chain comprising 1-2 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different X atoms; and

the bond labeled r is a single or a double bond.

25. The ICE inhibitor according to claim 23, wherein said scaffold has the formula:

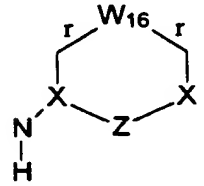
(IIB) 

wherein:

each X is independently C or N; and

Z is CO or SO_2.

26. The ICE inhibitor according to claim 23, wherein said scaffold has the formula:

(IIC) 

wherein:

each X is independently C or N;

Z is CO or SO_2;

W_{16} is a straight chain comprising 1-2 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising

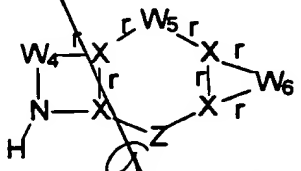
two ends which are covalently bound to two different C atoms through bonds r; and

each bond labeled r is independently a single or a double bond.

27. An ICE inhibitor comprising:

(a) a scaffold of formula III:

(III)



, wherein:

each X is independently C or N;

Z is CO or SO_2;

W_4 is a straight chain comprising 2-4 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different atoms;

W_5 is a direct bond or a straight chain comprising 1-2 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different X atoms through bonds r;

W_6 is a straight chain comprising 3-5 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different X atoms through bonds r;

each bond labeled r is independently a single or a double bond;

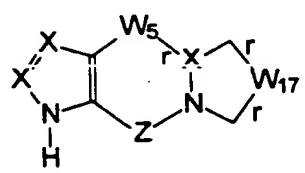
H is a first hydrogen bonding moiety and Z is a second hydrogen bonding moiety, each of said moieties being capable of forming a hydrogen bond with a different backbone atom of ICE, said backbone atom being selected from the group consisting of the carbonyl oxygen of Arg-341, the amide -NH- group of Arg-341, the carbonyl oxygen of Ser-339 and the amide -NH- group of Ser-339;

(b) a first and a second moderately hydrophobic moiety, said moieties each being covalently bound to said scaffold and each being capable of associating with a separate binding pocket of ICE when the inhibitor is bound thereto, said binding pocket being selected from the group consisting of the P2 binding pocket, the P3 binding pocket, the P4 binding pocket and the P' binding pocket; and

(c) an electronegative moiety comprising one or more electronegative atoms, said atoms being attached to the same atom or to adjacent atoms in the moiety and said moiety being covalently bound to said scaffold and being capable of forming one or more hydrogen bonds or salt bridges with residues in the P1 binding pocket of ICE.

28. The ICE inhibitor according to claim 27, wherein said scaffold has the formula:

(IIIA)



wherein:

each X is independently C or N;

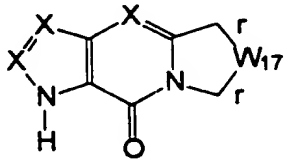
Z is CO or SO_2;

W_5 is a direct bond or a straight chain comprising 1-2 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different atoms;

W_{17} is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different C atoms through bonds r; and

each bond labeled r is independently a single or a double bond.

29. The ICE inhibitor according to claim 27, wherein:

(IIIB) 

wherein:

each X is independently C or N;

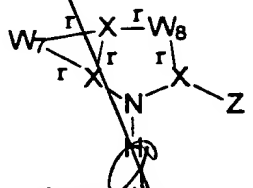
W_{17} is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different C atoms through bonds r; and

each bond labeled r is independently a

single or a double bond.

30. An ICE inhibitor comprising:

(a) a scaffold of formula IV:

(IV) 

wherein:

each X is independently C or N;

Z is CO or SO_2;

W_7 is a straight chain comprising 3-5 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different X atoms through bonds r;

W_8 is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated, and said chain comprising two ends which are covalently bound to two different X atoms through bonds r;

each bond labeled r is independently a single or a double bond;

H is a first hydrogen bonding moiety and Z is a second hydrogen bonding moiety, each of said moieties being capable of forming a hydrogen bond with a different backbone atom of ICE, said backbone atom being selected from the group consisting of the carbonyl oxygen of Arg-341, the amide -NH- group of Arg-341, the carbonyl oxygen of Ser-339 and the amide

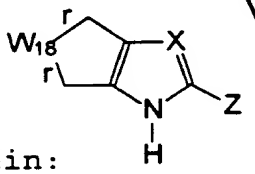
-NH- group of Ser-339;

(b) a first and a second moderately hydrophobic moiety, said moieties each being covalently bound to said scaffold and each being capable of associating with a separate binding pocket of ICE when the inhibitor is bound thereto, said binding pocket being selected from the group consisting of the P2 binding pocket, the P3 binding pocket, the P4 binding pocket and the P' binding pocket; and

(c) an electronegative moiety comprising one or more electronegative atoms, said atoms being attached to the same atom or to adjacent atoms in the moiety and said moiety being covalently bound to said scaffold and being capable of forming one or more hydrogen bonds or salt bridges with residues in the P1 binding pocket of ICE.

31. The ICE inhibitor according to claim 30, wherein said scaffold has the formula:

(IVA)



wherein:

each X is independently C or N;

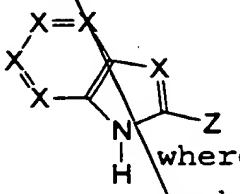
Z is CO or SO_2;

W_{18} is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different C atoms through bonds r; and

each bond labeled r is independently a

single or a double bond.

32. The ICE inhibitor according to claim 30, wherein said scaffold has the formula:

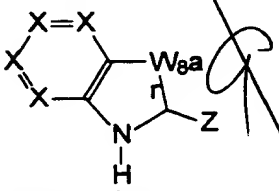
(IVB) 

wherein:

each X is independently C or N; and

Z is CO or SO_2.

33. The ICE inhibitor according to claim 30, wherein said scaffold has the formula:

(IVC) 

wherein:

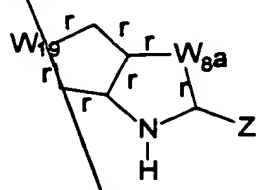
each X is independently C or N;

Z is CO or SO_2;

W_{8a} is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different C atoms; and

the bond labeled r is a single or a double bond.

34. The ICE inhibitor according to claim 30, wherein said scaffold has the formula:

(IVD) 

wherein:

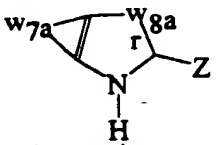
Z is CO or SO_2;

W_{8a} is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different C atoms through bonds r;

W_{19} is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different C atoms through bonds r; and

each bond labeled r is independently a single or a double bond.

35. The ICE inhibitor according to claim 30, wherein said scaffold has the formula:

(IVE) 

wherein:

Z is CO or SO_2;

W_{8a} is a straight chain comprising 1-3 covalently bound members independently selected from

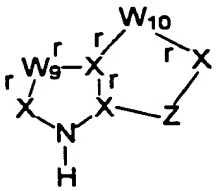
the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different C atoms;

W_{7a} is a straight chain comprising 3 covalently bound members independently selected from the group consisting of C, N, S and O, said chain comprising two ends which are covalently bound to two different C atoms to form an aryl ring therewith; and

the bond labeled r is a single or a double bond.

36. An ICE inhibitor comprising:

a) a scaffold of formula V:

(V) 

wherein:

each X is independently C or N;

Z is CO or SO_2;

W_9 is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different X atoms through bonds r;

W_{10} is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising

two ends which are covalently bound to two different X atoms through bonds r;

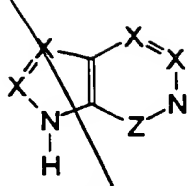
each bond labeled r is independently a single or a double bond;

H is a first hydrogen bonding moiety and Z is a second hydrogen bonding moiety, each of said moieties being capable of forming a hydrogen bond with a different backbone atom of ICE, said backbone atom being selected from the group consisting of the carbonyl oxygen of Arg-341, the amide -NH- group of Arg-341, the carbonyl oxygen of Ser-339 and the amide -NH- group of Ser-339;

b) a first and a second moderately hydrophobic moiety, said moieties each being covalently bound to said scaffold and each being capable of associating with a separate binding pocket of ICE when the inhibitor is bound thereto, said binding pocket being selected from the group consisting of the P2 binding pocket, the P3 binding pocket, the P4 binding pocket and the P' binding pocket; and

c) an electronegative moiety comprising one or more electronegative atoms, said atoms being attached to the same atom or to adjacent atoms in the moiety and said moiety being covalently bound to said scaffold and being capable of forming one or more hydrogen bonds or salt bridges with residues in the P1 binding pocket of ICE.

37. The ICE inhibitor according to claim 36, wherein said scaffold has the formula:

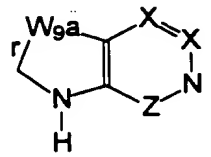
(VA) 

wherein:

each X is independently C or N; and

Z is CO or SO_2.

38. The ICE inhibitor according to claim 36, wherein said scaffold has the formula:

(VB) 

wherein:

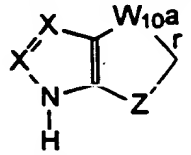
each X is independently C or N;

Z is CO or SO_2;

W_{9a} is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different C atoms; and

the bond labeled r is a single or a double bond.

39. The ICE inhibitor according to claim 36, wherein said scaffold has the formula:

(VC) 

wherein:

each X is independently C or N;

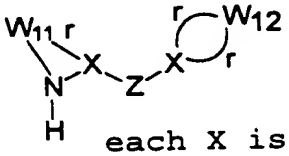
Z is CO or SO_2;

W_{10a} is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different X atoms; and

the bond labeled r is a single or a double bond.

40. An ICE inhibitor comprising:

(a) a scaffold of formula VI:

(VI) 

wherein:

each X is independently C or N;

Z is CO or SO_2;

W_{11} is a straight chain comprising 3-5 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different atoms to form a ring which may optionally be benzofused or pyridinofused;

W_{12} is a straight chain comprising 4-6 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to the indicated X atom through bonds r;

each bond labeled r is independently a

single or a double bond;

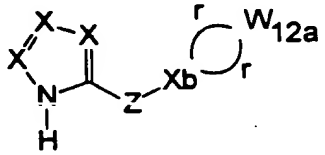
H is a first hydrogen bonding moiety and Z is a second hydrogen bonding moiety, each of said moieties being capable of forming a hydrogen bond with a different backbone atom of ICE, said backbone atom being selected from the group consisting of the carbonyl oxygen of Arg-341, the amide -NH- group of Arg-341, the carbonyl oxygen of Ser-339 and the amide -NH- group of Ser-339;

(b) a first and a second moderately hydrophobic moiety, said moieties each being covalently bound to said scaffold and each being capable of associating with a separate binding pocket of ICE when the inhibitor is bound thereto, said binding pocket being selected from the group consisting of the P2 binding pocket, the P3 binding pocket, the P4 binding pocket and the P' binding pocket; and

(c) an electronegative moiety comprising one or more electronegative atoms, said atoms being attached to the same atom or to adjacent atoms in the moiety and said moiety being covalently bound to said scaffold and being capable of forming one or more hydrogen bonds or salt bridges with residues in the P1 binding pocket of ICE.

41. The ICE inhibitor according to claim 40, wherein said scaffold has the formula:

(VIA)



wherein:

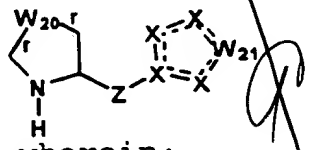
each X and X_b is independently C or N;

Z is CO or SO_2;

W_{12a} is a straight chain comprising 4-6 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to the indicated X_b atom through bonds r; and

each bond labeled r is independently a single or a double bond.

42. The ICE inhibitor according to claim 40, wherein said scaffold has the formula:

(VIB) 

wherein:

each X is independently C or N;

Z is CO or SO_2;

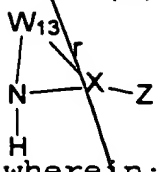
W_{20} is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different C atoms through bonds r;

W_{21} is a straight chain comprising 1-2 covalently bound members independently selected from the group consisting of C, N, S and O, said chain comprising two ends which are covalently bound to two different C atoms to form an aryl ring therewith; and

each bond labeled r is independently a single or a double bond.

43. An ICE inhibitor comprising:

(a) a scaffold of formula VII:

(VII) 

wherein:

X is C or N;

Z is CO or SO_2;

W_{13} is a straight chain comprising 3-5 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different atoms;

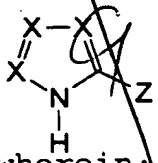
the bond labeled r is a single or a double bond;

H is a first hydrogen bonding moiety and Z is a second hydrogen bonding moiety, each of said moieties being capable of forming a hydrogen bond with a different backbone atom of ICE, said backbone atom being selected from the group consisting of the carbonyl oxygen of Arg-341, the amide -NH- group of Arg-341, the carbonyl oxygen of Ser-339 and the amide -NH- group of Ser-339;

(b) a first and a second moderately hydrophobic moiety, said moieties each being covalently bound to said scaffold and each being capable of associating with a separate binding pocket of ICE when the inhibitor is bound thereto, said binding pocket being selected from the group consisting of the P2 binding pocket, the P3 binding pocket, the P4 binding pocket and the P' binding pocket; and

(c) an electronegative moiety comprising one or more electronegative atoms, said atoms being attached to the same atom or to adjacent atoms in the moiety and said moiety being covalently bound to said scaffold and being capable of forming one or more hydrogen bonds or salt bridges with residues in the P1 binding pocket of ICE.

44. The ICE inhibitor according to claim 43, wherein said scaffold has the formula:

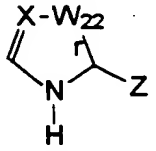
(VIIA) 

wherein:

each X is independently C or N; and

Z is CO or SO_2.

45. The ICE inhibitor according to claim 43, wherein said scaffold has the formula:

(VIIB) 

wherein:

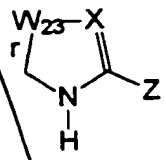
X is C or N;

Z is CO or SO_2;

W_{22} is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different atoms; and

the bond labeled r is a single or a double bond.

46. The ICE inhibitor according to claim 43, wherein said scaffold has the formula:

(VIIC) 

wherein:

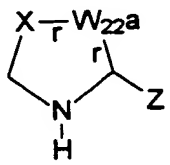
X is C or N;

Z is CO or SO_2;

W_{23} is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different atoms; and

the bond labeled r is a single or a double bond.

47. The ICE inhibitor according to claim 43, wherein said scaffold has the formula:

(VIID) 

wherein:

X is C or N;

Z is CO or SO_2;

W_{22a} is a straight chain comprising 1-3 covalently bound members independently selected from the group consisting of C, N, S and O, said covalent bonds between said members being independently saturated or unsaturated and said chain comprising two ends which are covalently bound to two different atoms through bonds r; and

each bond labeled r is independently a single or a double bond.

48. An ICE inhibitor comprising:

a) a scaffold comprising any monocyclic, bicyclic or tricyclic system, wherein each ring of said system comprises 5-7 members, said system comprising C, N, O or S, said system being aromatic or non-aromatic and comprising a central ring, wherein the distance between the centroid of said central ring and the alpha carbon of Cys-285 of ICE is between about 5.0Å and about 6.0Å when the inhibitor is bound to ICE and the distance between the centroid of said central ring and the alpha carbon of His-237 of ICE is between about 5.5Å and about 6.5Å when the inhibitor is bound to ICE;

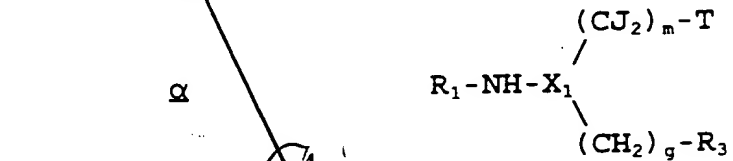
b) a first hydrogen bonding moiety and a second hydrogen bonding moiety, each of said moieties being capable of forming a hydrogen bond with a different backbone atom of ICE, said atoms being selected from the group consisting of the carbonyl oxygen of Arg-341, the amide -NH- group of Arg-341, the carbonyl oxygen of Ser-339 and the amide -NH- group of Ser-339;

c) a first and a second moderately hydrophobic moiety, said moieties each being covalently bound to said scaffold and each being capable of associating with a separate binding pocket of ICE when the inhibitor is bound thereto, said binding pocket being selected from the group consisting of the P2 binding pocket, the P3 binding pocket, the P4 binding pocket and the P' binding pocket; and

d) an electronegative moiety

comprising one or more electronegative atoms, said atoms being attached to the same atom or to adjacent atoms in the moiety and said moiety being covalently bound to said scaffold and being capable of forming one or more hydrogen bonds or salt bridges with residues in the P1 binding pocket of ICE.

49. A compound represented by the formula:



wherein:

X_1 is CH or N;

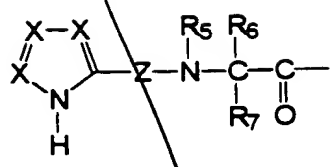
g is 0 or 1;

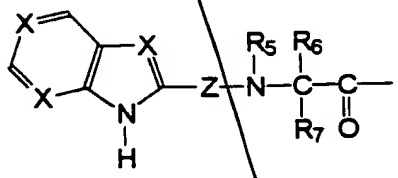
each J is independently selected from the group consisting of -H, -OH, and -F, provided that when a first and second J are bound to a C and said first J is -OH, said second J is -H;

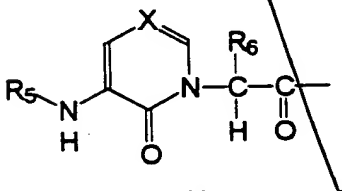
m is 0, 1, or 2;

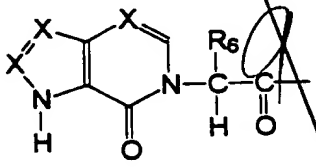
T is $-Ar_3$, -OH, $-CF_3$, $-CO-CO_2H$, $-CO_2H$ or any bioisosteric replacement for $-CO_2H$;

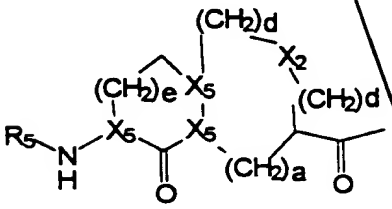
R_1 is selected from the group consisting of the following formulae, in which any ring may optionally be singly or multiply substituted at any carbon by Q_1, at any nitrogen by R_5, or at any atom by =O, -OH, $-CO_2H$, or halogen, and in which any saturated ring may optionally be unsaturated at one or two bonds:

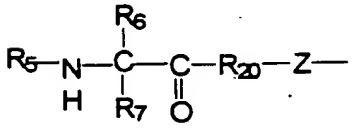
(a) 

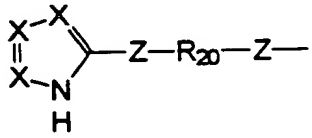
(b) 

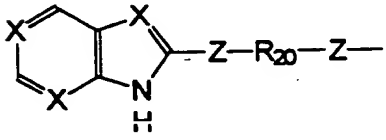
(C) 

(d) 

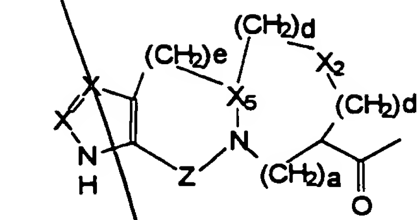
(e) 

(f) 

(g) 

(h) 

(i)



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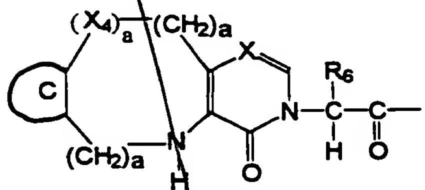
(j)



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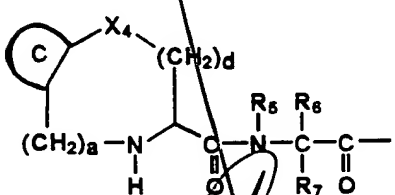
(k)



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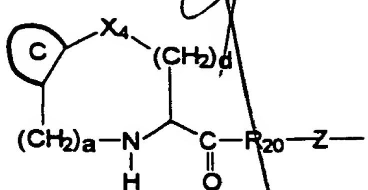
(l)



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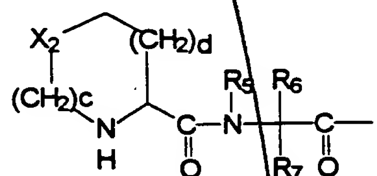
(m)



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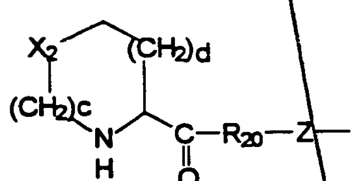
(n)



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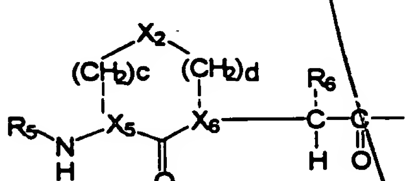
(o)



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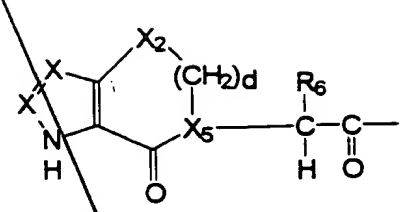
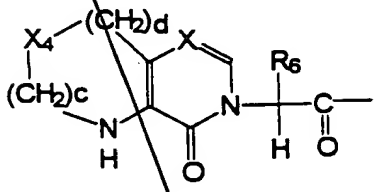
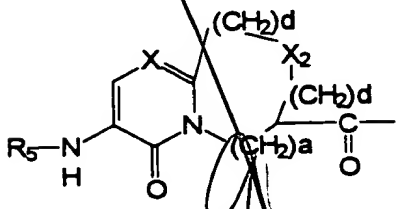
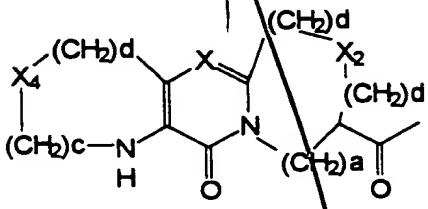
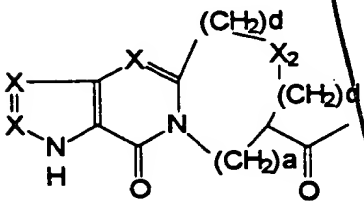
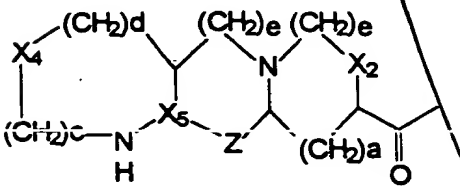
(p) 

(q) 

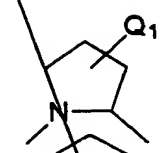
(r) 

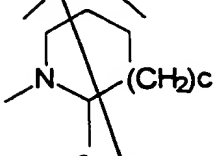
(s) 

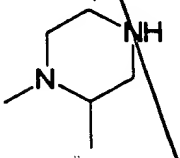
(t) 

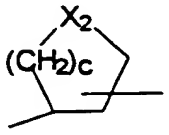
(v) 

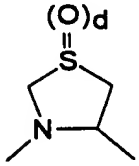
R_{20} is selected from the group consisting of:

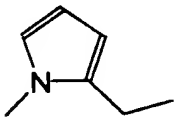
(aa1)  ;

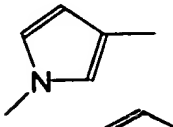
(aa2)  ;

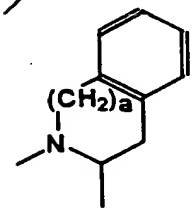
(aa3)  ;

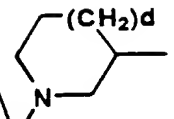
(aa4)  ;

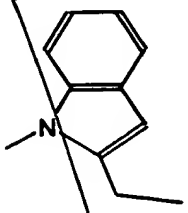
(aa5)  ;

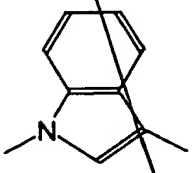
(bb)  ;

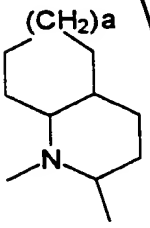
(cc)  ;

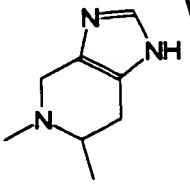
(dd)  ;

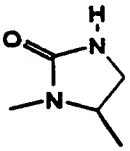
(ee)  ;

(ff)  ;

(gg)  ;

(gga)  ;

(ggb)  ;

(ggc)  ; and

wherein each ring C is independently chosen from the group consisting of benzo, pyrido, thieno, pyrrolo, furano, thiazolo, isothiazolo, oxazolo, isoxazolo, pyrimido, imidazolo, cyclopentyl, and cyclohexyl;

R_3 is
-CN,
$-CH=CH-R_9$,
$-CH=N-O-R_9$,
$-(CH_2)_{1-3}-T_1-R_9$,
$-CJ_2-R_9$,
$-CO-R_{13}$, or
$-CO-CO-N(R_5)(R_{10})$;

each R_4 is independently selected from the group consisting of:
-H,
$-Ar_1$,
$-R_9$,
$-T_1-R_9$, and
$-(CH_2)_{1,2,3}-T_1-R_9$,

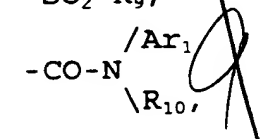
each T_1 is independently selected from the group consisting of:

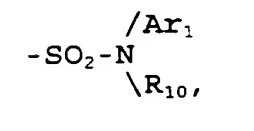
$-CH=CH-$,
-O-,
-S-,
-SO-,
$-SO_2-$,
$-NR_{10}-$,
$-NR_{10}-CO-$,
-CO-,
-O-CO-,
-CO-O-,
$-CO-NR_{10}-$,
$-O-CO-NR_{10}-$,
$-NR_{10}-CO-O-$,

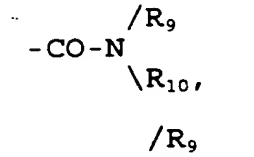
$-NR_{10}-CO-NR_{10}-$,
$-SO_2-NR_{10}-$,
$-NR_{10}-SO_2-$, and
$-NR_{10}-SO_2-NR_{10}-$,

each R_5 is independently selected from the group consisting of:

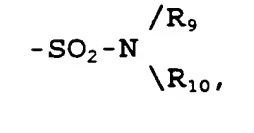
-H,
$-Ar_1$,
$-CO-Ar_1$,
$-SO_2-Ar_1$,
$-R_9$,
$-CO-R_9$,
$-CO-O-R_9$,
$-SO_2-R_9$,







and



R_6 and R_7 taken together form a saturated 4-8 member carbocyclic ring or heterocyclic ring containing -O-, -S-, or -NH-, or R_7 is -H and R_6 is

-H
$-Ar_1$,

$-R_9$, or
$-(CH_2)_{1,2,3}-T_1-R_9$,

each R_9 is a C_{1-6} straight or branched alkyl group optionally singly or multiply substituted by -OH, -F, or =O and optionally substituted with one or two Ar_1 groups;

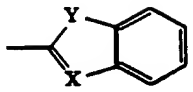
each R_{10} is independently selected from the group consisting of -H or a C_{1-6} straight or branched alkyl group;

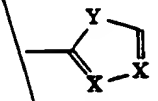
each R_{13} is independently selected from the group consisting of $-Ar_2$ and $-R_4$,

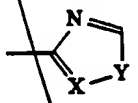
each Ar_1 is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings, a cycloalkyl group which contains between 3 and 15 carbon atoms and between 1 and 3 rings, said cycloalkyl group being optionally benzofused, and a heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocycle group containing at least one heteroatom group selected from -O-, -S-, -SO-, $-SO_2-$, =N-, and -NH-, said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by =O, -OH, perfluoro C_{1-3} alkyl, or $-Q_1$;

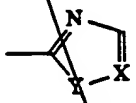
each Ar_2 is independently selected from the following group, in which any ring may optionally be

substituted by $-Q_1$:

(hh)  ,

(ii)  ,

(jj)  , and

(kk)  ;

Ar_3 is a cyclic group selected from the set consisting of a phenyl ring, a 5-membered heteroaromatic ring, and a 6-membered heteroaromatic ring, said heteroaromatic rings comprising 1-3 heteroatom groups selected from -O-, -S-, -SO-, $-SO_2-$, =N-, and -NH-, said cyclic group optionally being singly or multiply substituted with =O, -OH, halogen, perfluoro C_{1-3} alkyl, or $-CO_2H$;

each Q_1 is independently selected from the group consisting of

$-Ar_1$

$-R_9$,

$-T_1-R_9$, and

$-(CH_2)_{1,2,3}-T_1-R_9$,

provided that when $-Ar_1$ is substituted with a Q_1 group which comprises one or more additional $-Ar_1$ groups, said additional $-Ar_1$ groups are not substituted with Q_1;

each X is independently selected from the group consisting of =N-, and =CH-;

each X_2 is independently selected from the group consisting of -O-, $-CH_2-$, -NH-, -S-, -SO-, and $-SO_2-$;

each X_3 is independently selected from the group consisting of $-CH_2-$, -S-, -SO-, and $-SO_2-$;

each X_4 is independently selected from the group consisting of $-CH_2-$ and -NH-;

each X_5 is independently selected from the group consisting of -CH- and -N-;

X_6 is CH or N, provided that when X_6 is N in the R_1 group labeled (o) and X_5 is CH and X_2 is CH_2 the ring of the R_1 group labeled (o) must be substituted by Q_1 or benzofused;

each Y is independently selected from the group consisting of -O- and -S-;

each Z is independently CO or SO_2,

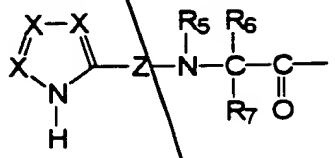
each a is independently 0 or 1,

each c is independently 1 or 2,

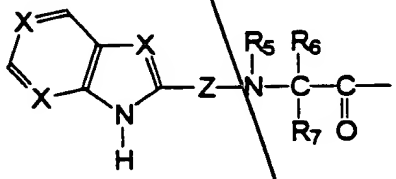
each d is independently 0, 1, or 2, and

each e is independently 0, 1, 2, or 3.

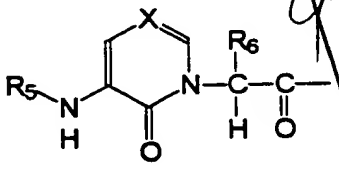
50. The compound according to claims 49 or 80, wherein R_1 is:

(a) 

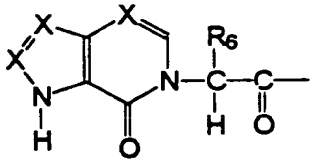
51. The compound according to claims 49 or 80, wherein R_1 is:

(b) 

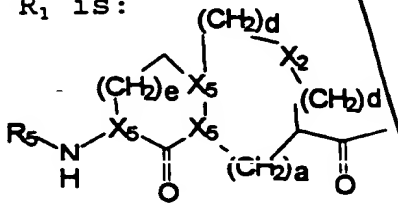
52. The compound according to claims 49 or 80, wherein R_1 is:

(c) 

53. The compound according to claims 49 or 80, wherein R_1 is:

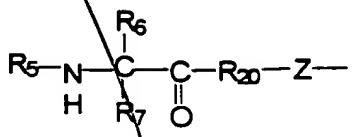
(d) 

54. The compound according to claims 49 or 80, wherein R_1 is:

(e) 

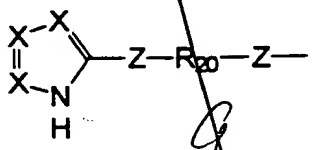
55. The compound according to claims 49 or 80, wherein R_1 is:

(f)



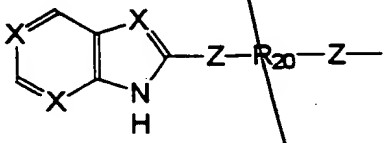
56. The compound according to claims 49 or 80, wherein R_1 is:

(g)



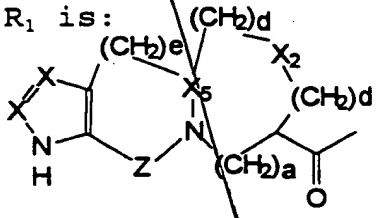
57. The compound according to claims 49 or 80, wherein R_1 is:

(h)



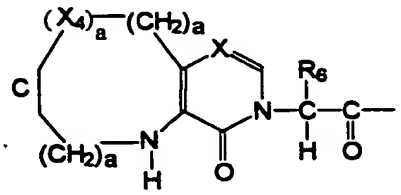
58. The compound according to claims 49 or 80, wherein R_1 is:

(i)

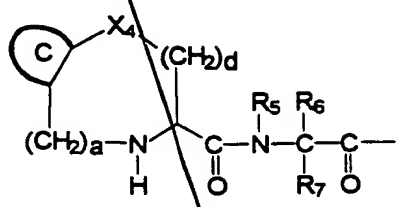


59. The compound according to claims 49 or 80, wherein R_1 is:

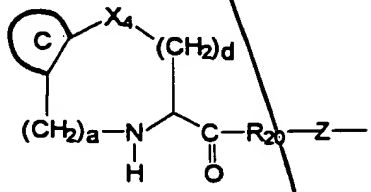
(j)



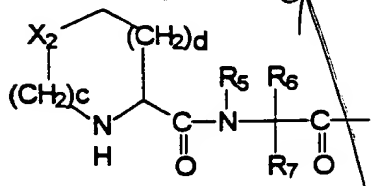
60. The compound according to claims 49 or 80, wherein R_1 is:

(k) 

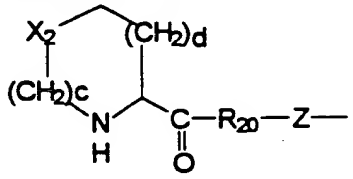
61. The compound according to claims 49 or 80, wherein R_1 is:

(l) 

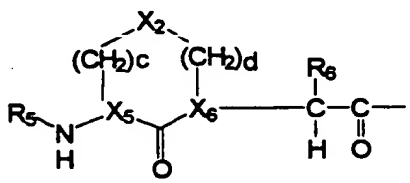
62. The compound according to claims 49 or 80, wherein R_1 is:

(m) 

63. The compound according to claims 49 or 80, wherein R_1 is:

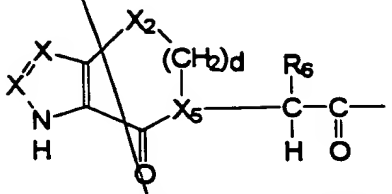
(n) 

64. The compound according to claims 49 or 80, wherein R_1 is:

(o) 

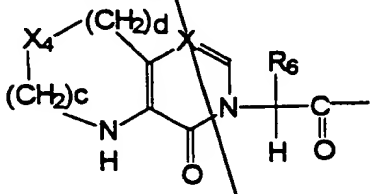
65. The compound according to claims 49 or 80, wherein R_1 is:

(p)



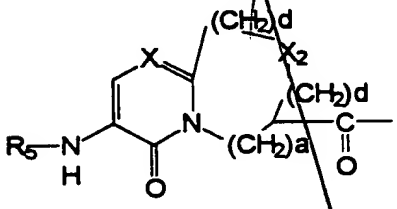
66. The compound according to claims 49 or 80, wherein R_1 is:

(q)



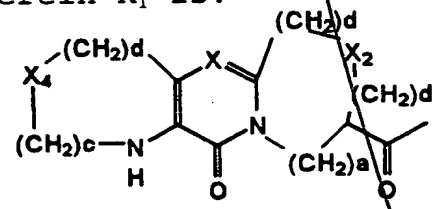
67. The compound according to claims 49 or 80, wherein R_1 is:

(r)



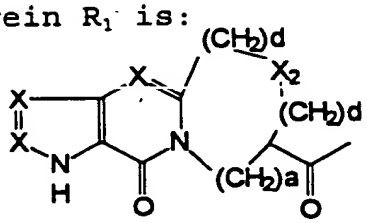
68. The compound according to claims 49 or 80, wherein R_1 is:

(s)



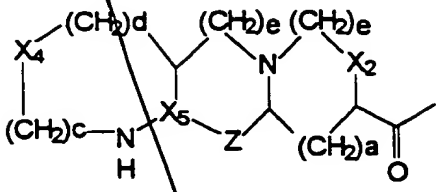
69. The compound according to claims 49 or 80, wherein R_1 is:

(t)



70. The compound according to claims 49 or 80, wherein R_1 is:

(v)



71. A pharmaceutical composition for treating or preventing an IL-1 mediated disease comprising a pharmaceutically effective amount of an ICE inhibitor according to any one of claims 1-70 and 80-124 and a pharmaceutically acceptable carrier.

72. A pharmaceutical composition for treating or preventing an autoimmune disease comprising a pharmaceutically effective amount of an ICE inhibitor according to any one of claims 1-70 and 80-124 and a pharmaceutically acceptable carrier.

73. A pharmaceutical composition for treating or preventing an inflammatory disease comprising a pharmaceutically effective amount of an ICE inhibitor according to any one of 1-70 and 80-124 and a pharmaceutically acceptable carrier.

74. A pharmaceutical composition for treating or preventing a neurodegenerative disease comprising a pharmaceutically effective amount of an ICE inhibitor according to any one of claims 1-70 and 80-124 and a pharmaceutically acceptable carrier.

75. A pharmaceutical composition for inhibiting an ICE-mediated function comprising a pharmaceutically effective amount of an ICE inhibitor according to any one of claims 1-70 and 80-124 and a pharmaceutically acceptable carrier.

76. A method for treating or preventing a disease selected from the group consisting of IL-1 mediated disease, autoimmune disease, inflammatory disease and neurodegenerative disease in a patient comprising the step of administering to said patient a pharmaceutical composition according to any one of claims 71 to 75.

77. A method for selecting an ICE inhibitor comprising the steps of:

a) selecting a candidate compound of defined chemical structure comprising at least two hydrogen bonding moieties, at least two moderately hydrophobic moieties and one electronegative moiety comprising one or more electronegative atoms attached either to the same atom or to adjacent atoms in the electronegative moiety;

b) determining a low-energy conformation for binding of said compound to the active site of ICE;

c) evaluating the capability of said compound in said conformation to form at least two hydrogen bonds with the non-carbon backbone atoms of Arg-341 and Ser-339 of ICE;

d) evaluating the capability of said compound in said conformation to associate with at least two of the binding pockets of ICE selected from the group consisting of the P2 binding pocket, the P3

binding pocket, the P4 binding pocket and the P' binding pocket;

e) evaluating the capability of said compound in said conformation to interact with the P1 binding pocket of ICE; and

f) accepting or rejecting said candidate compound as an ICE inhibitor based on the determinations and evaluations carried out in the preceeding steps.

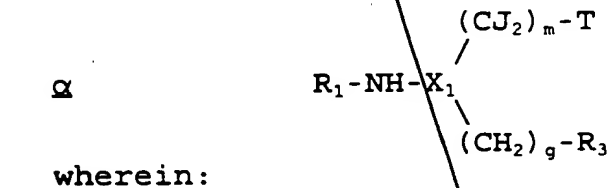
78. The method of claim 77, additionally comprising the following steps which follow step e) and precede step f):

g) evaluating the deformation energy of binding of said compound to ICE; and

h) evaluating the contribution of the sum of all electrostatic interactions between said compound and ICE when said compound is bound thereto in said conformation.

79. An ICE inhibitor selected by either of the methods according to claims 77 or 78.

80. A compound represented by the formula:



wherein:

X_1 is -CH;

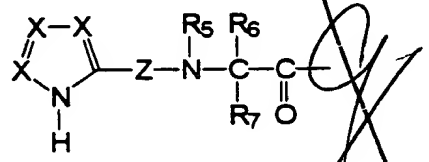
g is 0 or 1;

each J is independently selected from the group consisting of -H, -OH, and -F, provided that when a first and second J are bound to a C and said first J is -OH, said second J is -H;

m is 0, 1, or 2;

T is -OH, -CO-CO_2H, -CO_2H, or any bioisosteric replacement for -CO_2H;

R_1 is selected from the group consisting of the following formulae, in which any ring may optionally be singly or multiply substituted at any carbon by Q_1, at any nitrogen by R_5, or at any atom by =O, -OH, -CO_2H, or halogen; any saturated ring may optionally be unsaturated at one or two bonds; and wherein R_1 (e) and R_1 (y) are optionally benzofused;

(a) 
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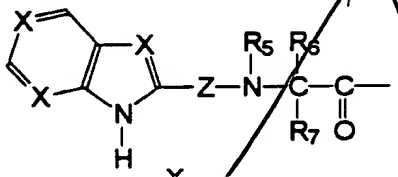
(b) 
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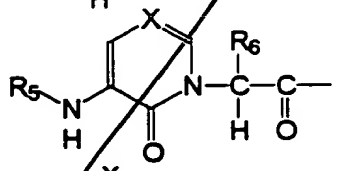
(c) 
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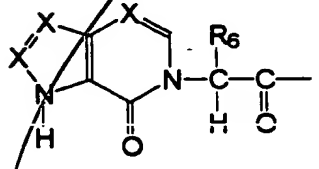
(d) 
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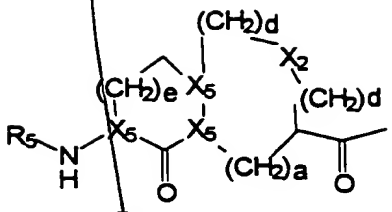
(e) 

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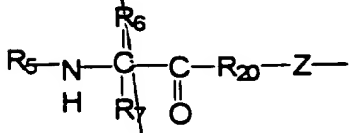
(f) 

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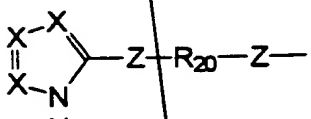
(g) 

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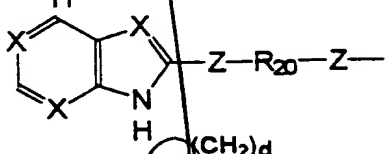
(h) 

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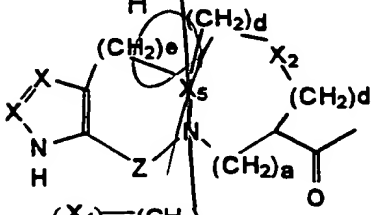
(i) 

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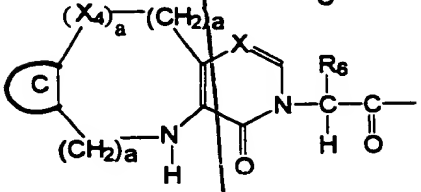
(j) 

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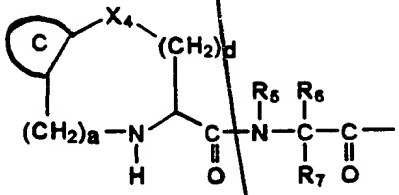
(k) 

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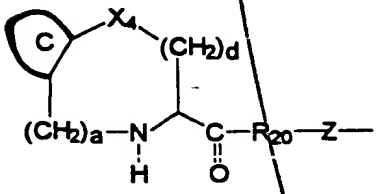
(l) 

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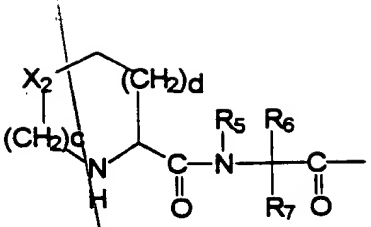
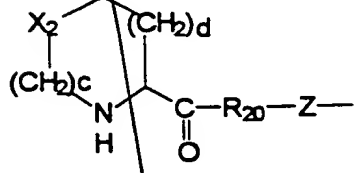
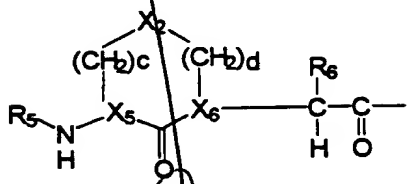
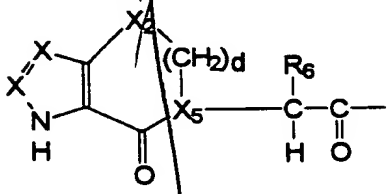
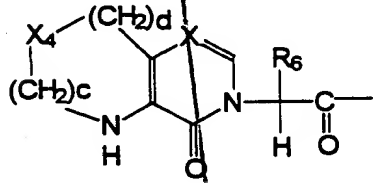
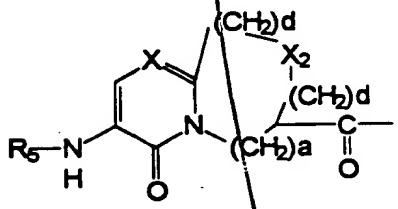
(m) 

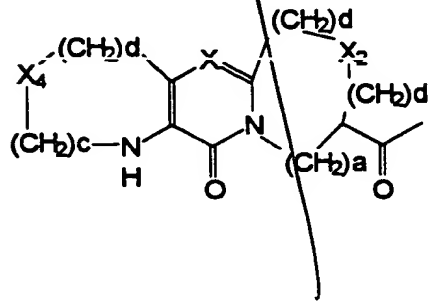
(n) 

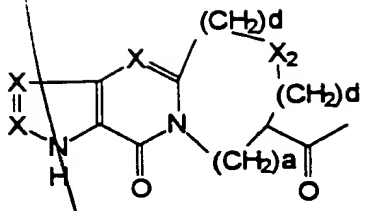
(o) 

(p) 

(q) 

(r) 

(s) 

(t) 

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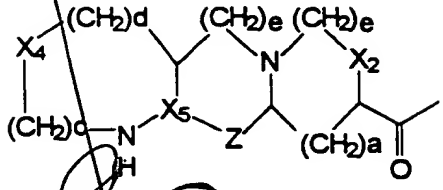
(v) 

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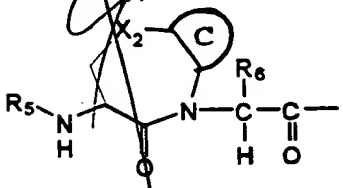
(w) 

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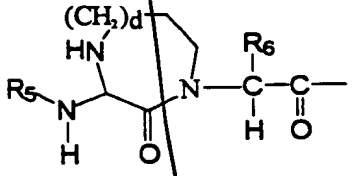
(x) 

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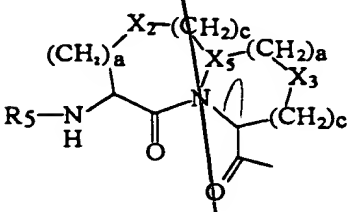
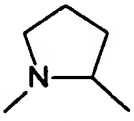
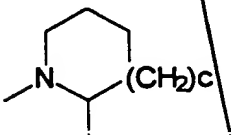
(y) 

;

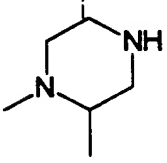
R_{20} is selected from the group consisting of:

(aa1) 

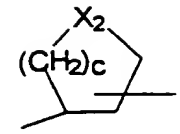
;

(aa2) 

;

(aa3) 

;

(aa4) 

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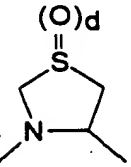
(aa5) 

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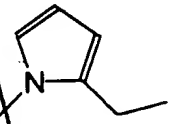
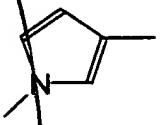
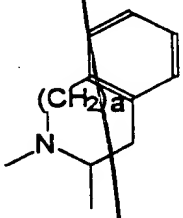
(bb) 

;

(cc) 

;

(dd) 

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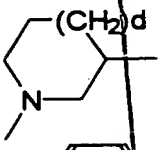
(ee) 

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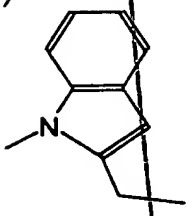
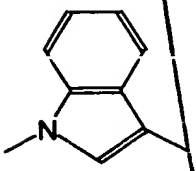
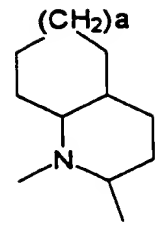
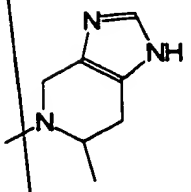
(ff) 

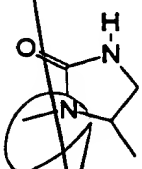
;

(gg) 

;

(gga)  ;

(ggb)  ; and

(ggc) 

wherein each ring C is independently chosen from the group consisting of benzo, pyrido, thieno, pyrrolo, furano, thiazolo, isothiazolo, oxazolo, isoxazolo, pyrimido, imidazolo, cyclopentyl, and cyclohexyl;

R_3 is:

-CN,

$-CH=CH-R_9$,

$-CH=N-O-R_9$,

$-(CH_2)_{1-3}-T_1-R_9$,

$-CJ_2-R_9$,

$-CO-R_{13}$, or

$-CO-CO-N\begin{matrix}/R_5\\ \backslash R_{10}\end{matrix}$;

each R_4 is independently selected from the group consisting of:

-H,

$-Ar_1$,

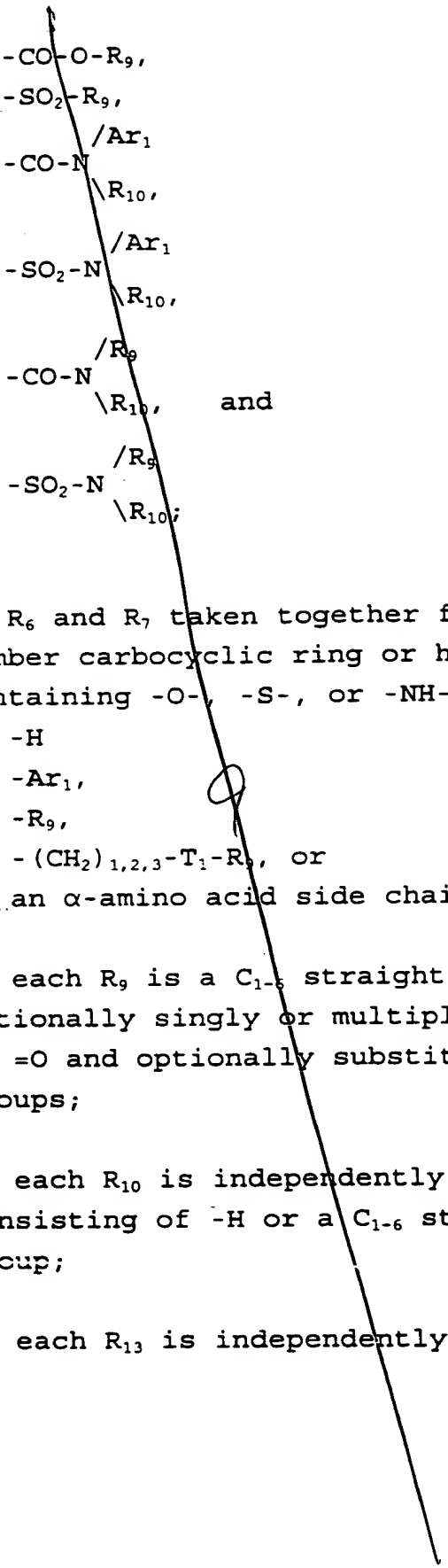
$-R_9$,
$-T_1-R_9$, and
$-(CH_2)_{1,2,3}-T_1-R_9$;

each T_1 is independently selected from the group consisting of:

$CH=CH-$,
$-O-$,
$-S-$,
$-SO-$,
$-SO_2-$,
$-NR_{10}-$,
$-NR_{10}-CO-$,
$-CO-$,
$-O-CO-$,
$-CO-O-$,
$-CO-NR_{10}-$,
$-O-CO-NR_{10}-$,
$-NR_{10}-CO-O-$,
$-NR_{10}-CO-NR_{10}-$,
$-SO_2-NR_{10}-$,
$-NR_{10}-SO_2-$, and
$-NR_{10}-SO_2-NR_{10}-$;

each R_5 is independently selected from the group consisting of:

$-H$,
$-Ar_1$,
$-CO-Ar_1$,
$-SO_2-Ar_1$,
$-CO-NH_2$,
$-SO_2-NH_2$,
$-R_9$,
$-CO-R_9$,



$-CO-O-R_9$,

$-SO_2-R_9$,

$-CO-N(Ar_1)(R_{10})$,

$-SO_2-N(Ar_1)(R_{10})$,

$-CO-N(R_9)(R_{10})$, and

$-SO_2-N(R_9)(R_{10})$;

R_6 and R_7 taken together form a saturated 4-8 member carbocyclic ring or heterocyclic ring containing -O-, -S-, or -NH-; or R_7 is -H and R_6 is

-H

$-Ar_1$,

$-R_9$,

$-(CH_2)_{1,2,3}-T_1-R_9$, or

an α-amino acid side chain residue;

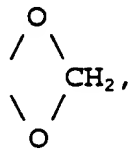
each R_9 is a C_{1-6} straight or branched alkyl group optionally singly or multiply substituted by -OH, -F, or =O and optionally substituted with one or two Ar_1 groups;

each R_{10} is independently selected from the group consisting of -H or a C_{1-6} straight or branched alkyl group;

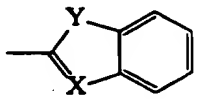
each R_{13} is independently selected from the group

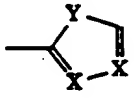
consisting of $-Ar_2$, $-R_4$ and $-N(R_5)-OH$;

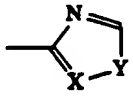
each Ar_1 is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings, a cycloalkyl group which contains between 3 and 15 carbon atoms and between 1 and 3 rings, said cycloalkyl group being optionally benzofused, and a heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocycle group containing at least one heteroatom group selected from -O-, -S-, -SO-, $-SO_2-$, =N-, and -NH-, said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by $-NH_2$, $-CO_2H$, -Cl, -F, -Br, -I, $-NO_2$, -CN,

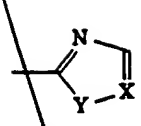
=O, -OH, -perfluoro C_{1-3} alkyl,  , or $-Q_1$;

each Ar_2 is independently selected from the following group, in which any ring may optionally be singly or multiply substituted by $-Q_1$ and $-Q_2$:

(hh)  ;

(ii)  ;

(jj)  ; and

(kk)  ;

each Q_1 is independently selected from the group consisting of:

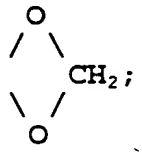
$-Ar_1$

$-O-Ar_1$

$-R_9$,

$-T_1-R_9$, and

$-(CH_2)_{1,2,3}-T_1-R_9$;

each Q_2 is independently selected from the group consisting of -OH, $-NH_2$, $-CO_2H$, -Cl, -F, -Br, -I, $-NO_2$, -CN, $-CF_3$, and  ;

provided that when $-Ar_1$ is substituted with a Q_1 group which comprises one or more additional $-Ar_1$ groups, said additional $-Ar_1$ groups are not substituted with Q_1;

each X is independently selected from the group consisting of =N-, and =CH-;

each X_2 is independently selected from the group consisting of -O-, $-CH_2-$, -NH-, -S-, -SO-, and $-SO_2-$;

each X_3 is independently selected from the group consisting of $-CH_2-$, -S-, -SO-, and $-SO_2-$;

each X_4 is independently selected from the group consisting of $-CH_2-$ and -NH-;

each X_5 is independently selected from the group consisting of -CH- and -N-;

X_6 is -CH- or -N-;

each Y is independently selected from the group consisting of -O-, -S-, and -NH;

each Z is independently CO or SO_2;

each a is independently 0 or 1;

each c is independently 1 or 2;

each d is independently 0, 1, or 2; and

each e is independently 0, 1, 2, or 3;

provided that when

R_1 is (f),

R_6 is an α-amino acid side chain residue, and

R_7 is -H,

then (aa1) and (aa2) must be substituted with Q_1;

also provided that when

R_1 is (o),

g is 0,

J is -H,

m is 1,

R_6 is an α-amino acid side chain residue,

R_7 is -H,

X_2 is $-CH_2-$,

X_5 is -CH- ,

X_6 is -N- , and

R_3 is $-CO-N\begin{matrix}/R_{10}\\ \backslash R_{10}\end{matrix}$, or $-CO-R_{13}$, when

R_{13} is:

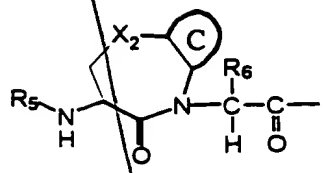
$-CH_2-O-CO-Ar_1$,
$-CH_2-S-CO-Ar_1$,
$-CH_2-O-Ar_1$,
$-CH_2-S-Ar_1$, or
$-R_4$ when $-R_4$ is -H;

then the ring of the R_1(o) group must be substituted with Q_1 or benzofused; and

provided that when
R_1 is (w),
g is 0,
J is -H,
m is 1,
T is $-CO_2H$,
X_2 is O,
R_5 is benzyloxycarbonyl, and
ring C is benzo,
then R_3 cannot be $-CO-R_{13}$ when:
R_{13} is $-CH_2-O-Ar_1$ and
Ar_1 is 1-phenyl-3-trifluoromethyl-pyrazole-5-yl wherein the phenyl is optionally substituted with a chlorine atom;
or when
R_{13} is $-CH_2-O-CO-Ar_1$, wherein
Ar_1 is 2,6-dichlorophenyl.

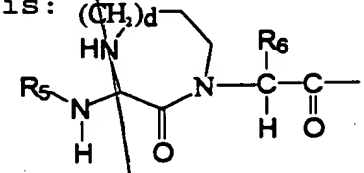
81. The compound according to claim 80, wherein R_1 is:

(w)



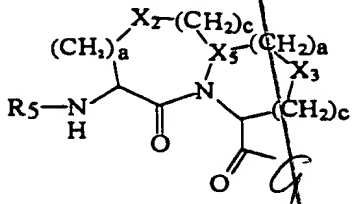
82. The compound according to claim 80, wherein R_1 is:

(x)



83. The compound according to claim 80, wherein R_1 is:

(y)



84. The compound according to claim 80, wherein:

X_1 is -CH;

g is 0;

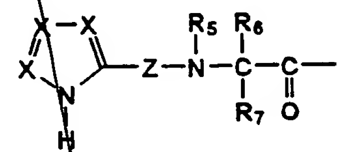
J is -H;

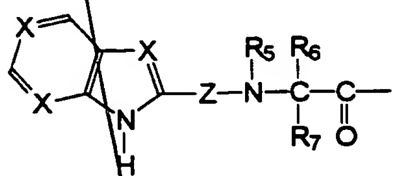
m is 0 or 1 and T is $-CO-CO_2H$, or any bioisosteric replacement for $-CO_2H$, or

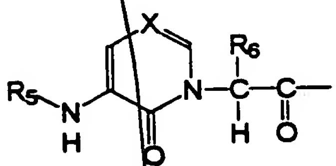
m is 1 and T is $-CO_2H$;

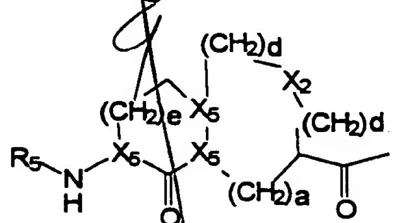
R_1 is selected from the group consisting of the following formulae, in which any ring may optionally be singly or multiply substituted at any carbon by

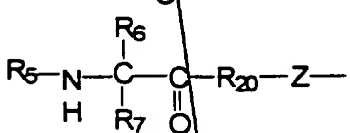
Q_1, at any nitrogen by R_5, or at any atom by =O, -OH, $-CO_2H$, or halogen, and wherein (e) is optionally benzofused:

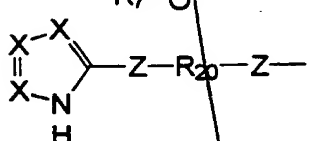
(a)  ,

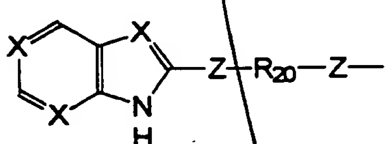
(b)  ,

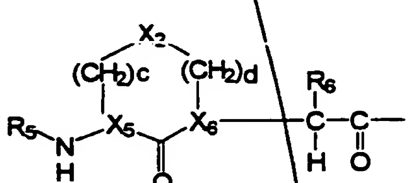
(c)  ,

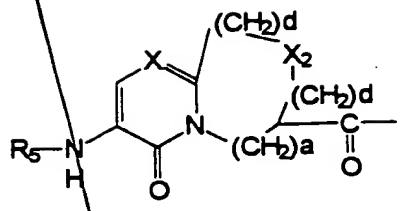
(e)  ,

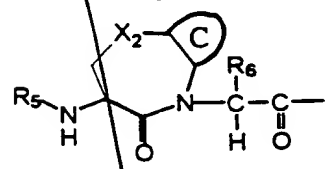
(f)  ,

(g)  ,

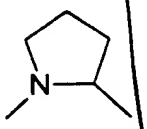
(h)  ,

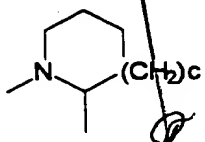
(o)  ,

(r)  , or

(w)  ;

R_{20} is:

(aa1)  , or

(aa2) 

and c is 1;

ring C is benzo optionally substituted with $-C_{1-3}$ alkyl, $-O-C_{1-3}$ alkyl, -Cl, -F or $-CF_3$;

when R_1 is (a) or (b), R_5 is preferably -H, and

when R_1 is (c), (e), (f), (o), (r), (w), (x) or (y), R_5 is preferably:

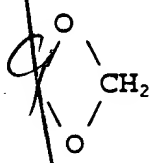
$-CO-Ar_1$
$-SO_2-Ar_1$,
$-CO-NH_2$,
$-CO-NH-Ar_1$
$-CO-R_9$,
$-CO-O-R_9$,

$-SO_2-R_9$, or
$-CO-NH-R_9$,

R_7 is -H and R_6 is: -H,
$-R_9$, or
$-Ar_1$;

R_9 is a C_{1-6} straight or branched alkyl group optionally substituted with =O and optionally substituted with $-Ar_1$;

R_{10} is -H or a $-C_{1-3}$ straight or branched alkyl group;

Ar_1 is phenyl, naphthyl, pyridyl, benzothiazolyl, thienyl, benzothienyl, benzoxazolyl, 2-indanyl, or indolyl substituted with $-O-C_{1-3}$ alkyl, $-NH-C_{1-3}$ alkyl, $-N-(C_{1-3}$ alkyl$)_2$, -Cl, -F, $-CF_3$, $-C_{1-3}$ alkyl, or  ;

Q_1 is R_9 or $-(CH_2)_{0,1,2}-T_1-(CH_2)_{0,1,2}-Ar_1$, wherein T_1 is -O- or -S-;

each X is independently selected from the group consisting of =N-, and =CH-;

each X_2 is independently selected from the group consisting of -O-, $-CH_2-$, -NH-, -S-, -SO-, and $-SO_2-$;

each X_5 is independently selected from the group consisting of -CH- and -N-;

X_6 is -CH- or -N-,

provided that when:

R_1 is R_1(o),

X_2 is $-CH_2-$,

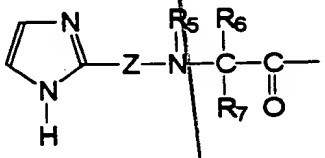
X_5 is -CH- , and

X_6 is -N- ,

then the ring of the R_1(o) group must be substituted with Q_1 or benzofused; and

Z is C=O.

85. The compound according to claim 84, wherein the R_1 group is

(a2) 

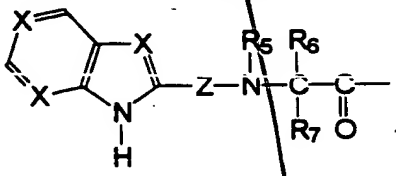
optionally substituted with Q_1, wherein

R_5 is -H;

R_7 is -H; and

Z is C=O.

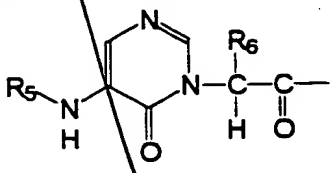
86. The compound according to claim 84, wherein the R_1 group is

(b) 

optionally substituted with Q_1, wherein

R_5 is -H;
R_7 is -H; and
Z is C=O.

87. The compound according to claim 84, wherein the R_1 group is

(c1) 

which is optionally substituted with Q_1;

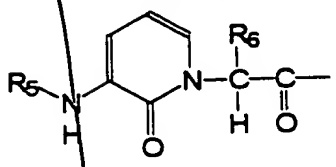
provided that when R_1 is (c1),

g is 0,
J is -H,
m is 1,
T is $-CO_2H$,
X is N,
R_5 is benzyloxycarbonyl, and
R_6 is -H,

then R_3 cannot be $-CO-R_{13}$ when
R_{13} is $-CH_2-O-Ar_1$ and
Ar_1 is 1-phenyl-3-trifluoromethyl-pyrazole-5-yl, wherein the phenyl is optionally substituted with a chlorine atom; or when

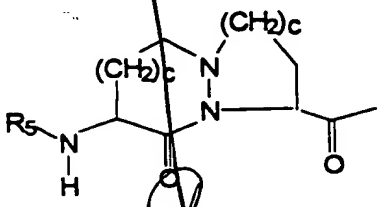
R_{13} is $-CH_2-O-CO-Ar_1$, wherein
Ar_1 is 2,6-dichlorophenyl,
and when the 2-position of the scaffold ring is substituted with para-fluoro-phenyl.

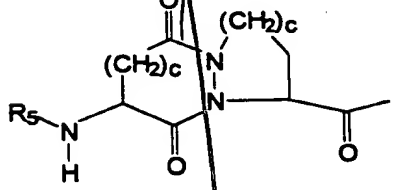
88. The compound according to claim 84, wherein the R_1 group is:

(c2)  ,

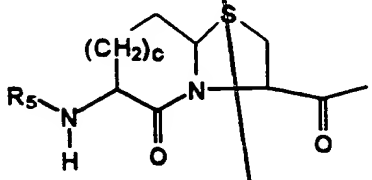
which is optionally substituted with Q_1.

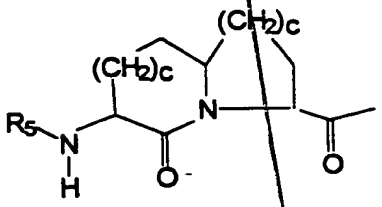
89. The compound according to claim 84, wherein the R_1 group is:

(e1)  ,

(e2)  ,

and c is 2; or

(e4)  , or

(e7)  ,

which is optionally benzofused,

and c is 1 or 2;

provided that when R_1 is (e4),

g is 0,
J is -H,
m is 1,
T is $-CO_2H$,
R_5 is benzyloxycarbonyl, and
c is 1,

then R_3 cannot be $-CO-R_{13}$ when
R_{13} is $-CH_2-O-Ar_1$ and
Ar_1 is 1-phenyl-3-trifluoromethyl-pyrazole-5-yl, wherein the phenyl is optionally substituted with a chlorine atom; or when

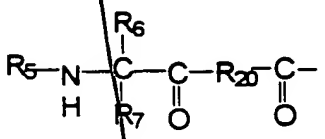
R_{13} is $-CH_2-O-CO-Ar_1$, wherein
Ar_1 is 2,6-dichlorophenyl,
and when the 2-position of the scaffold ring is substituted with para-fluoro-phenyl; and

also provided that when
R_1 is (e7),
g is 0,
J is -H,
m is 1,
T is $-CO_2H$ or -CO-NH-OH,
R_5 is a protective group for the N atom of an amino acid side chain residue, and
each c is 1,

then R_3 cannot be $-CO-R_{13}$ when
R_{13} is:
$-CH_2-O-CO-Ar_1$,
$-CH_2-S-CO-Ar_1$,
$-CH_2-O-Ar_1$, or
$-CH_2-S-Ar_1$.

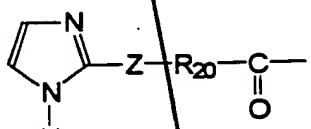
90. The compound according to claim 84, wherein the R_1 group is

(f1)



91. The compound according to claim 84, wherein the R_1 group is

(g2)



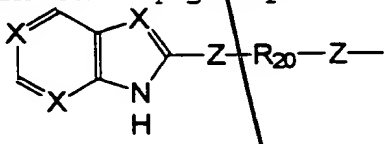
, wherein

R_{20} is (aa1) optionally substituted singly or multiply with Q_1; and

Z is C=O.

92. The compound according to claim 84, wherein the R_1 group is

(h)



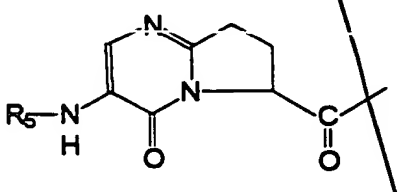
, wherein

R_{20} is (aa1) optionally substituted singly or multiply with Q_1; and

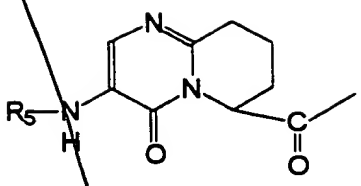
Z is C=O.

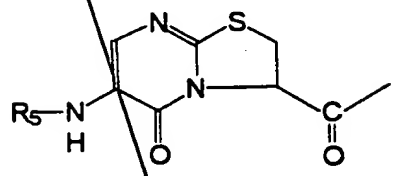
93. The compound according to claim 84, wherein the R_1 group is:

(r3)



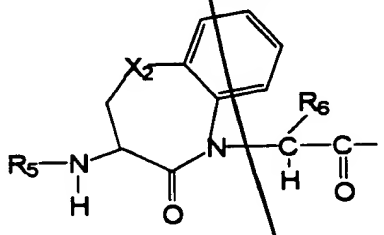
;

(r4)  ;

(r5)  ; and

optionally substituted with Q_1.

94. The compound according to claim 84, wherein the R_1 group is

(w1)  ; wherein

X_2 is:

-O- ,

-S- ,

$-SO_2-$, or

-NH-;

optionally substituted with R_5 or Q_1 at X_2 when X_2 is -NH-; and

ring C is benzo substituted with $-C_{1-3}$ alkyl, $-O-C_{1-3}$ alkyl, -Cl, -F or $-CF_3$.

95. The compound according to claim 84, wherein

R_3 is:

-CO-R_{13}, or

-CO-CO-N-R_9
R_{10};

T_1 is:

-O- or

-S-;

R_9 is a C_{1-6} straight or branched alkyl group optionally substituted with =O and optionally substituted with Ar_1; and

R_{13} is:

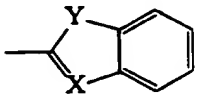
-H,

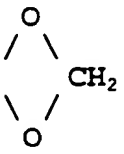
-R_9,

-Ar_2, or

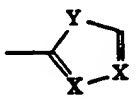
-CH_2-T_1-R_9.

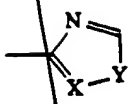
96. The compound according to claim 95, wherein -Ar_2 is:

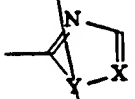
(hh) 

optionally substituted singly or multiply with -C_{1-6} alkyl, -O-C_{1-6} alkyl, -NH-C_{1-6} alkyl, -N-(C_{1-6} alkyl)$_2$, -S-C_{1-6} alkyl, -Cl, -F, -CF_3, or  .

97. The compound according to claim 95, wherein -Ar_2 is:

(ii) 

(jj)  , or

(kk) 

98. The compound according to claim 95, wherein:

R_{13} is $-CH_2-O-R_9$; wherein:

R_9 is a C_{1-6} straight or branched alkyl group optionally substituted with =O and optionally substituted with Ar_1.

99. The compound according to claim 95, wherein:

R_{13} is $-CH_2-S-R_9$; wherein:

R_9 is a C_{1-6} straight or branched alkyl group optionally substituted with Ar_1.

100. The compound according to claim 98, wherein:

R_{13} is $-CH_2-O-R_9$; wherein:

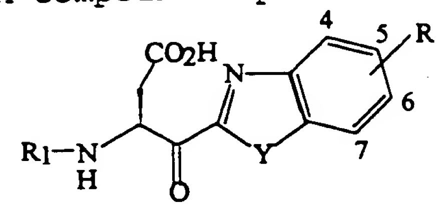
R_9 is a C_{1-6} straight or branched alkyl group optionally substituted with Ar_1.

101. The compound according to claim 95, wherein:

R_{13} is H.

102. A compound represented by the formula:

α



wherein the ring is optionally substituted with one or more R groups, preferably 0, 1 or 2; and wherein:

R_1 is R_5-(A)$_p$-;

R_5 is selected from the group consisting of:

-H,

-Ar_1,

-CO-Ar_1,

-SO_2-Ar_1,

-R_9,

-CO-R_9,

-CO-O-R_9,

-SO_2-R_9,

-CO-N(/Ar_1)(\R_{10}),

-SO_2-N(/Ar_1)(\R_{10}),

-CO-N(/R_9)(\R_{10}), and

-SO_2-N(/R_9)(\R_{10});

each A is independently selected from the group consisting of any α-amino acid;

p is 0, 1, 2, 3 or 4;

Y is

-O-,

-S- or

-NH; and

R is:

-H,

-O-C_{1-6} alkyl,

-NH(C_{1-6} alkyl),

-N(C_{1-6} alkyl)$_2$,

-S-C_{1-6} alkyl,

-C_{1-6} alkyl, or

-Q_2;

each R_9 is a C_{1-6} straight or branched alkyl group optionally singly or multiply substituted by -OH, -F, or =O and optionally substituted with one Ar_1 group;

each R_{10} is independently selected from the group consisting of -H or a C_{1-6} straight or branched alkyl group;

each T_1 is independently selected from the group consisting of:

-CH=CH-,

-O-,

-S-,

-SO-,

-SO_2-,

-NR_{10}-,

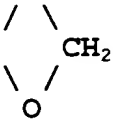
-NR_{10}-CO-,

-CO-,

-O-CO-,

-CO-O-,
-CO-NR_{10}-,
-O-CO-NR_{10}-,
-NR_{10}-CO-O-,
-NR_{10}-CO-NR_{10}-,
-SO_2-NR_{10}-,
-NR_{10}-SO_2-, and
-NR_{10}-SO_2-NR_{10}-,

each Ar_1 is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings, a cycloalkyl group which contains between 3 and 15 carbon atoms and between 1 and 3 rings, said cycloalkyl group being optionally benzofused, and a heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocycle group containing at least one heteroatom group selected from -O-, -S-, -SO-, -SO_2-, =N-, and -NH-, said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by -NH_2, -CO_2H, -Cl, -F, -Br, -I, -NO_2, -CN, =O, -OH, -perfluoro C_{1-3} alkyl,



or $-Q_1$;

each Q_1 is independently selected from the group consisting of:

-Ar_1
-R_9,
-T_1-R_9, and

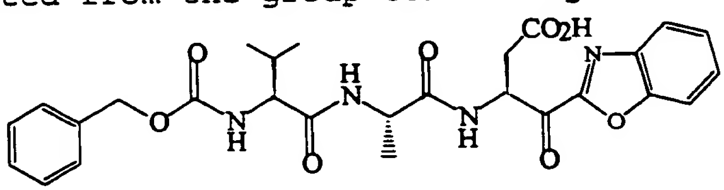
$-(CH_2)_{1,2,3}-T_1-R_9$;

each Q_2 is independently selected from the group consisting of -OH, $-NH_2$, $-CO_2H$, -Cl, -F, -Br, -I, $-NO_2$, -CN, $-CF_3$, and

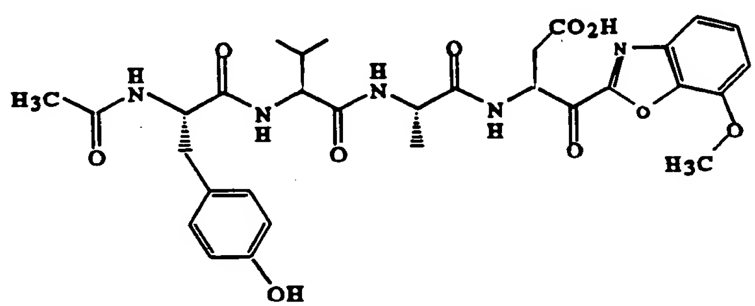
```
 O
/ \
   CH2;
\ /
 O
```

provided that when $-Ar_1$ is substituted with a Q_1 group which comprises one or more additional $-Ar_1$ groups, said additional $-Ar_1$ groups are not substituted with Q_1.

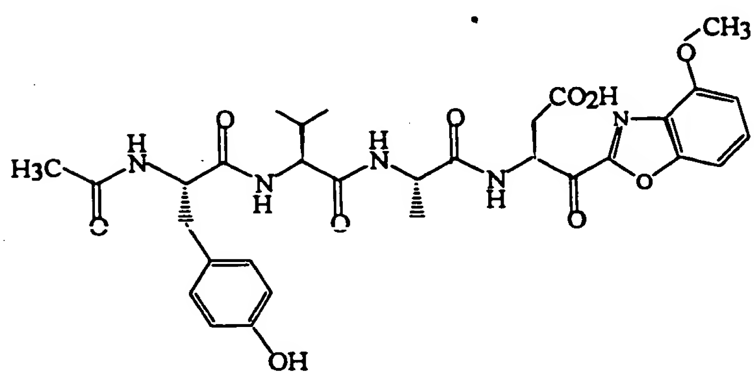
103. A compound according to claim 102 selected from the group consisting of:

(Q) 

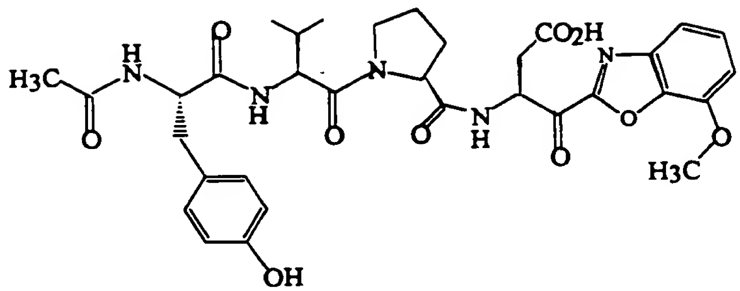
;

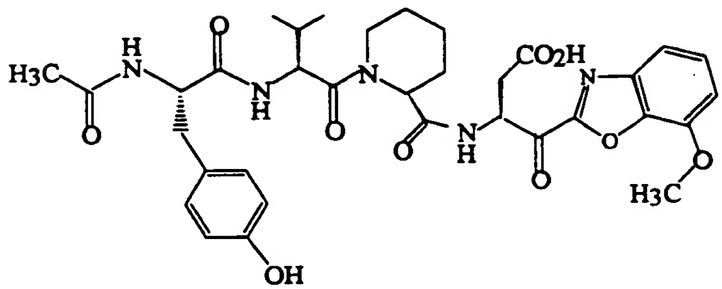
(R) 

;

(S) 

;

(T)  ; and

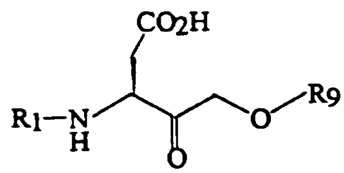
(V)  .

104. A compound according to claim 102 wherein each A is independently selected from the group consisting of the α-amino acids:

alanine,
histidine,
lysine,
phenylalanine,
proline,
tyrosine,
valine,
leucine,
isoleucine,
glutamine,
methionine,
homoproline,
3-(2-thienyl) alanine, and
3-(3-thienyl) alanine.

105. A compound represented by the formula:

II



wherein:

R_1 is R_5-$(A)_p$-;

each T_1 is independently selected from the group consisting of:

-CH=CH-,

-O-,

-S-,

-SO-,

-SO_2-,

-NR_{10}-,

-NR_{10}-CO-,

-CO-,

-O-CO-,

-CO-O-,

-CO-NR_{10}-,

-O-CO-NR_{10}-,

-NR_{10}-CO-O-,

-NR_{10}-CO-NR_{10}-,

-SO_2-NR_{10}-,

-NR_{10}-SO_2-, and

-NR_{10}-SO_2-NR_{10}-;

R_5 is selected from the group consisting of:

-H,

-Ar_1,

-CO-Ar_1,

-SO_2-Ar_1,

-R_9,

$-CO-R_9$,

$-CO-O-R_9$,

$-SO_2-R_9$,

$-CO-N(Ar_1)(R_{10})$,

$-SO_2-N(Ar_1)(R_{10})$,

$-CO-N(R_9)(R_{10})$, and

$-SO_2-N(R_9)(R_{10})$;

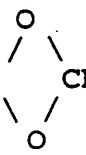
each A is independently selected from the group consisting of any α-amino acid;

p is 0, 1, 2, 3 or 4;

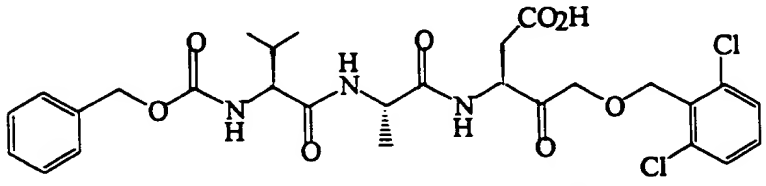
each R_9 is a C_{1-6} straight or branched alkyl group optionally singly or multiply substituted by -OH, -F, or =O and optionally substituted with an Ar_1 group;

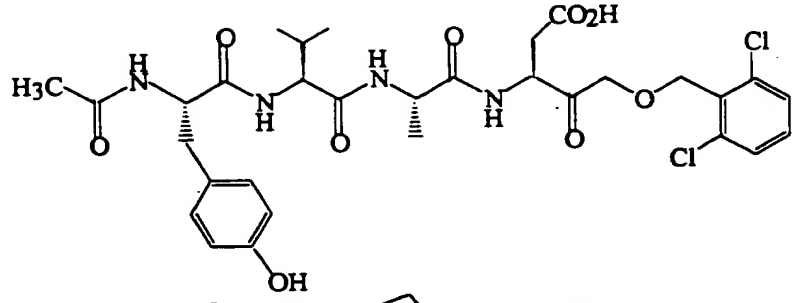
each R_{10} is independently selected from the group consisting of -H or a C_{1-6} straight or branched alkyl group;

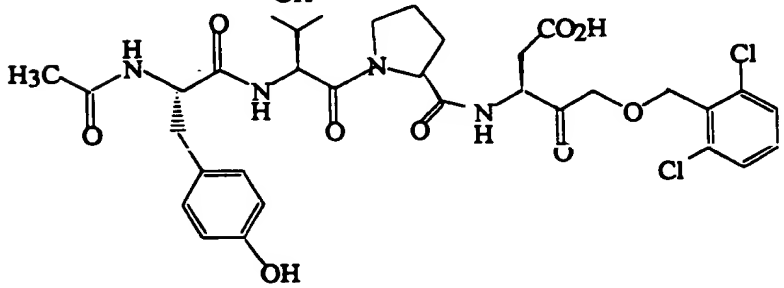
Ar_1 is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings, a cycloalkyl group which contains between 3 and 15 carbon atoms and between 1 and 3 rings, said cycloalkyl group being optionally benzofused, and a

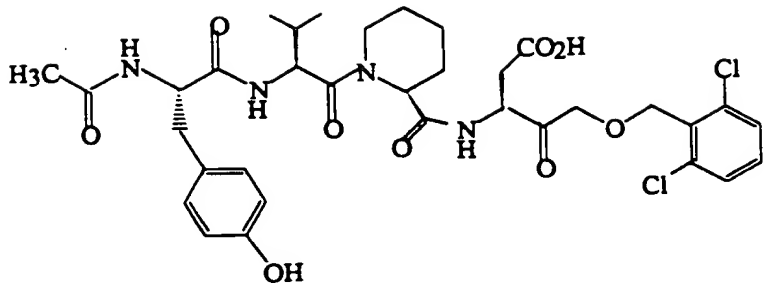
heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocycle group containing at least one heteroatom group selected from -O-, -S-, -SO-, $-SO_2-$, =N-, and -NH-, said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by $-NH_2$, $-CO_2H$, -Cl, -F, -Br, -I, $-NO_2$, -CH, =O, -OH, -perfluoro C_{1-3} alkyl,  , $-R_9$, or $-T_1-R_9$.

106. A compound according to claim 105 selected from the group consisting of:

(W)  ;

(X)  ;

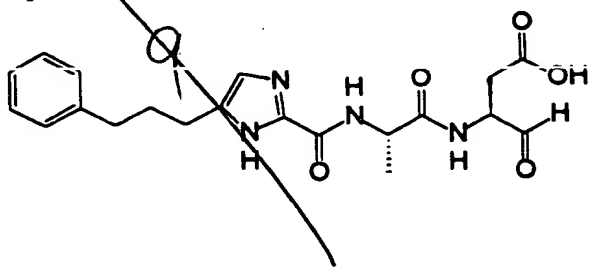
(Y)  ; and

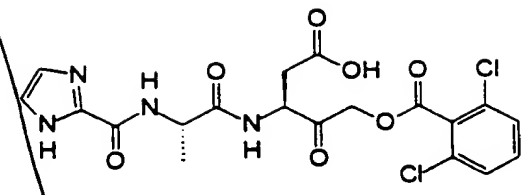
(Z) 

107. A compound according to claim 105 wherein each A is independently selected from the group consisting of the α-amino acids:

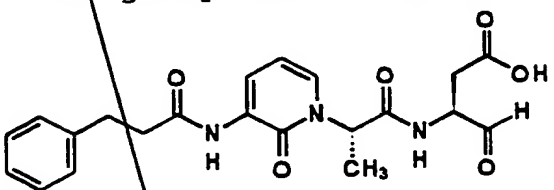
alanine,
histidine,
lysine,
phenylalanine,
proline,
tyrosine,
valine,
leucine,
isoleucine,
glutamine,
methionine,
homoproline,
3-(2-thienyl) alanine, and
3-(3-thienyl) alanine.

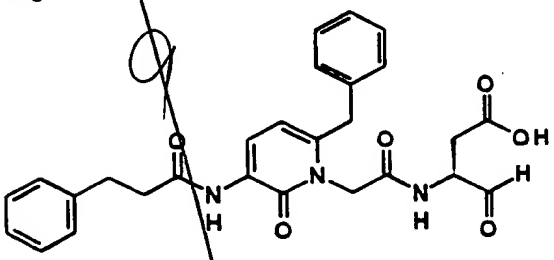
108. The compound according to claim 85, selected from the group consisting of:

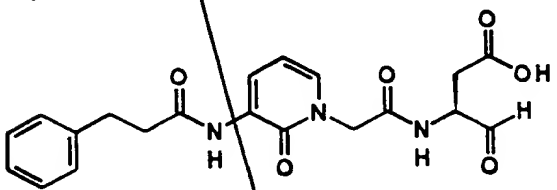
20d  ; and

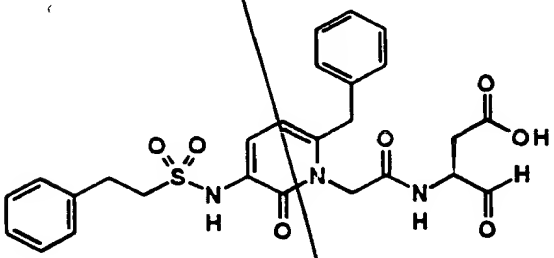
142 

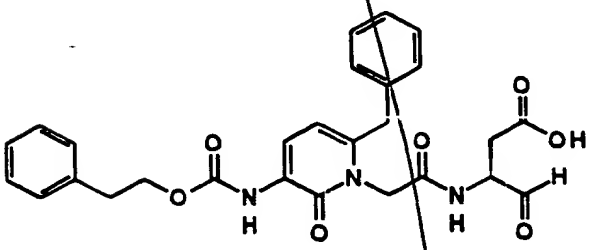
109. The compound according to claim 88, selected from the group consisting of

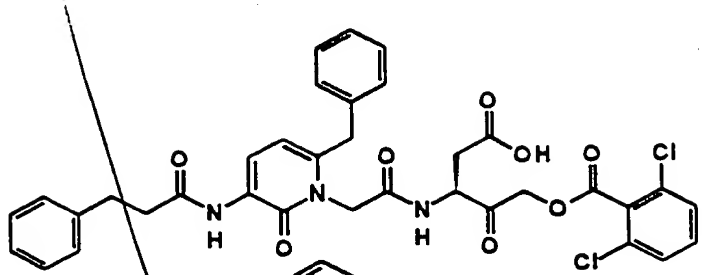
54a  ;

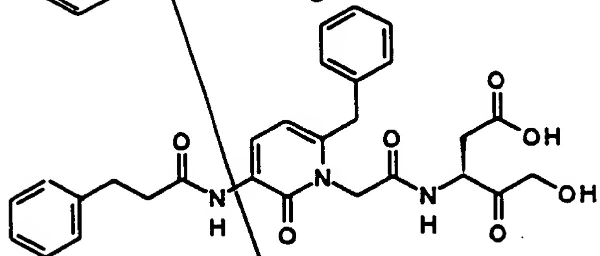
54b  ;

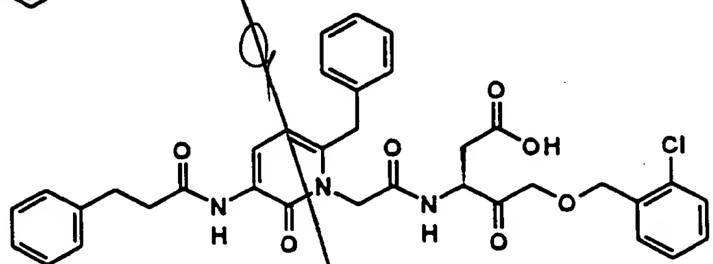
54g  ;

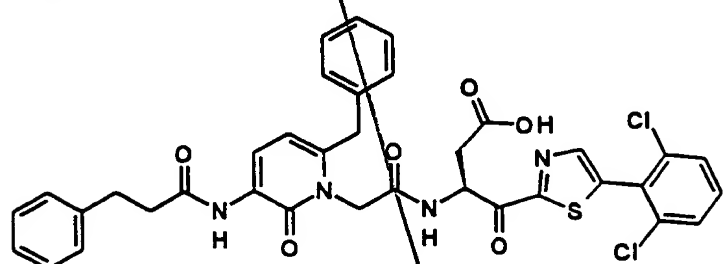
54j  ;

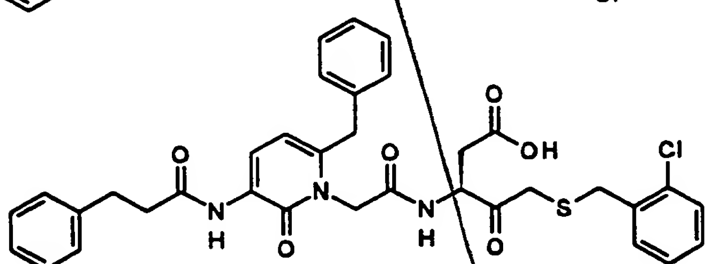
54k  ;

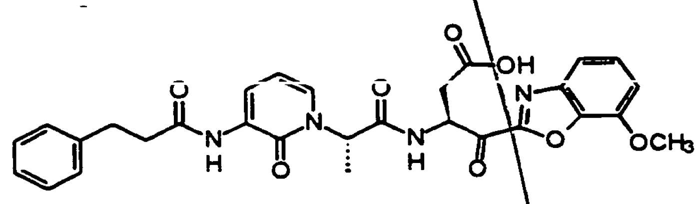
57b  ;

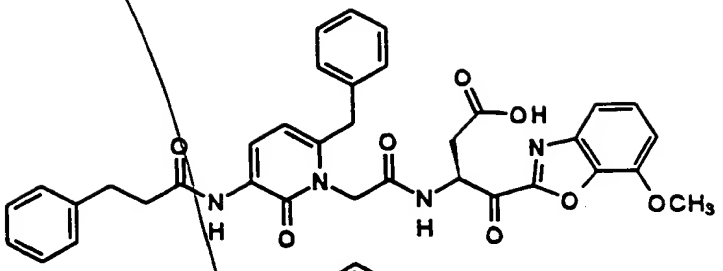
88  ;

90  ;

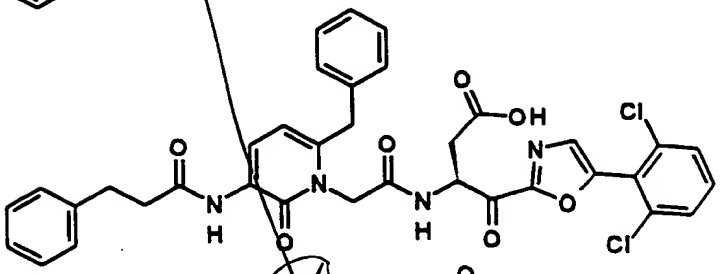
91  ;

125a  ;

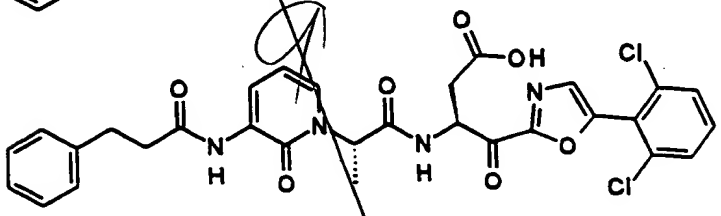
126  ;

127 

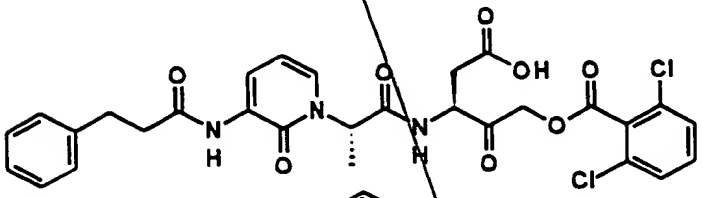
;

128 

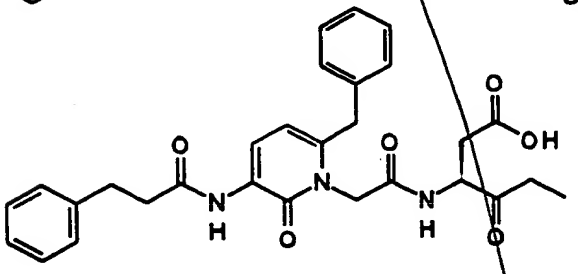
;

129 

;

130 

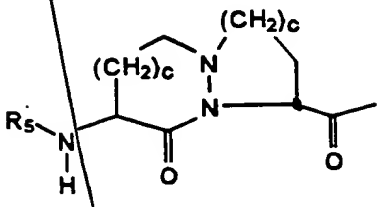
; and

131 

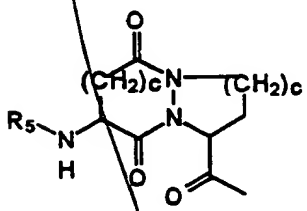
.

110. The compound according to claim 89, wherein:

R_1 is:

(e1) 

, or

(e2) 

,

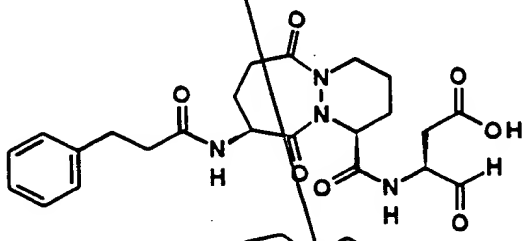
and c is 2;

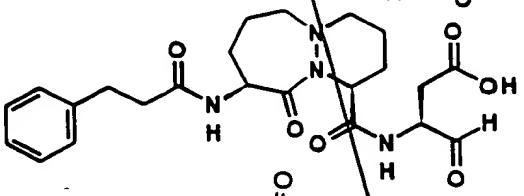
m is 1;

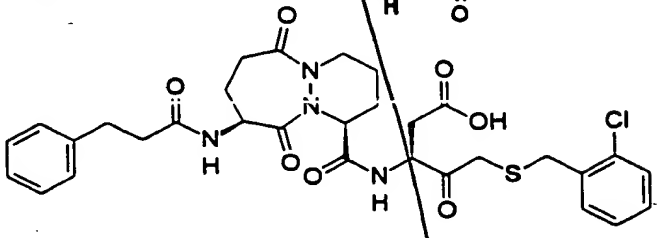
T is $-CO_2H$; and

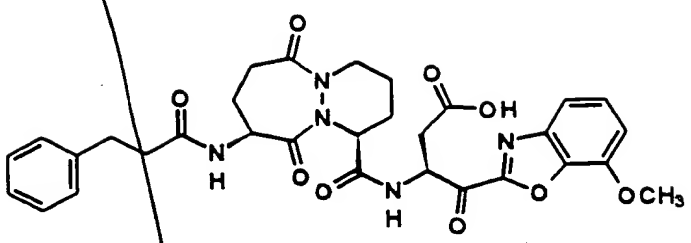
R_3 is $-CO-R_{13}$.

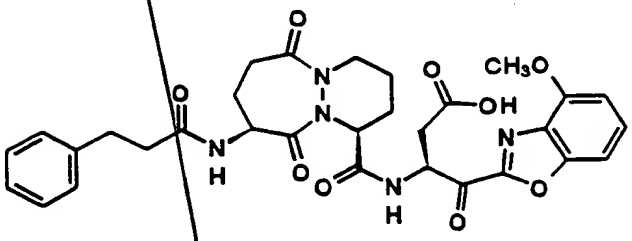
111. The compound according to claim 110, selected from the group consisting of:

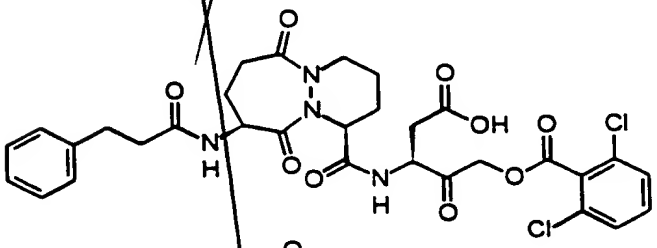
47a  ;

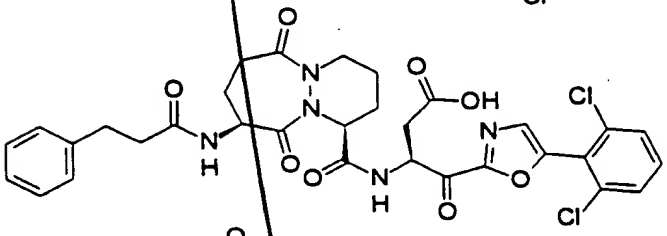
47b  ;

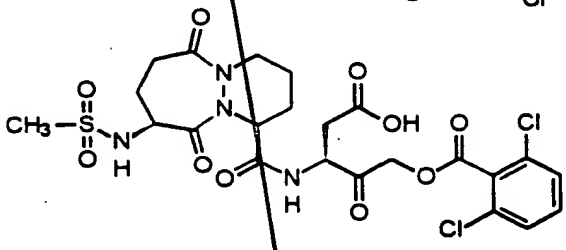
125b  ;

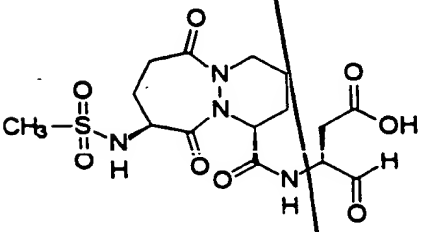
135a  ;

135b  ;

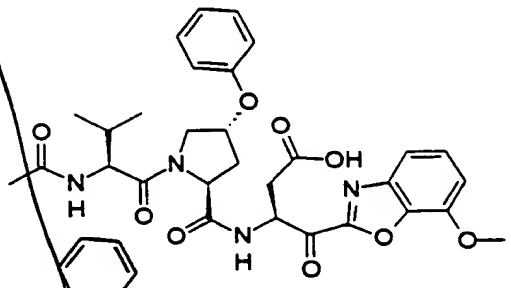
136  ;

137  ;

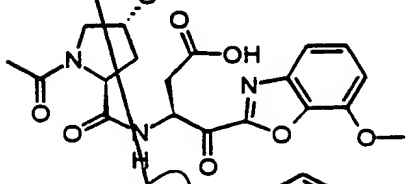
138  ; and

139 

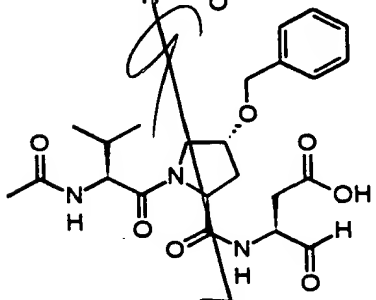
112. The compound according to claim 90, selected from the group consisting of:

86 

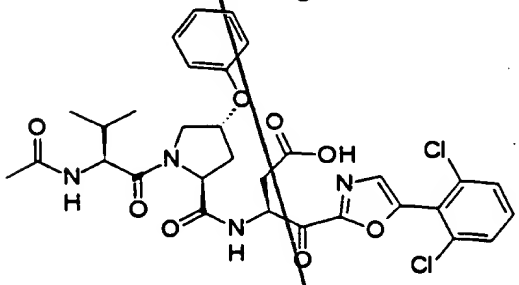
;

87 

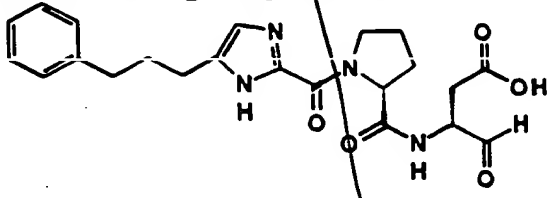
;

158 

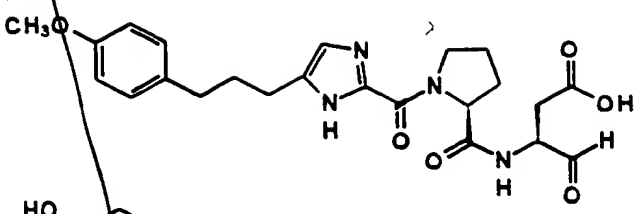
; and

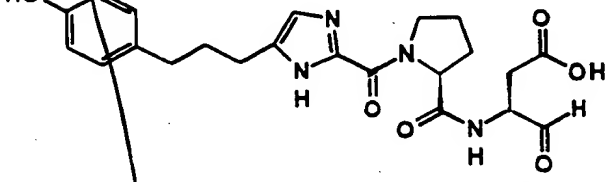
160 

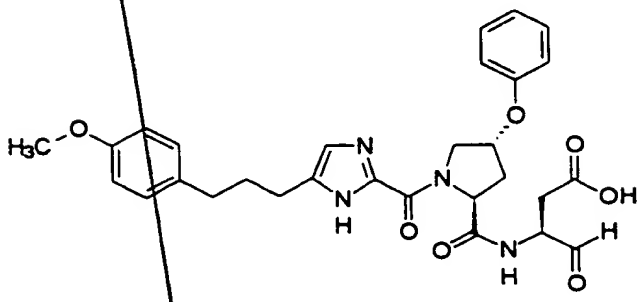
113. The compound according to claim 91, selected from the group consisting of:

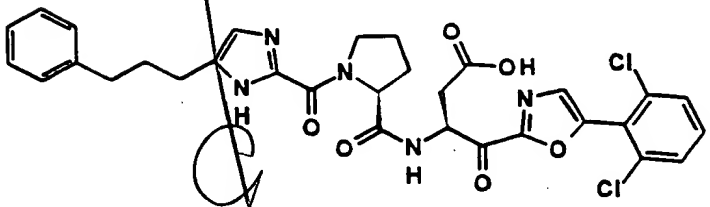
21d 

;

21e  ;

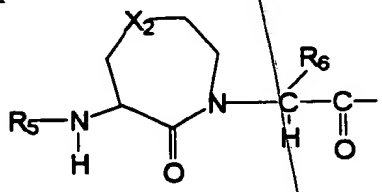
21f  ;

22e  ; and

157  .

114. The compound according to claim 84, wherein:

R_1 is:

(o6) 

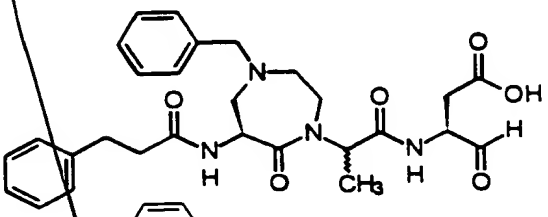
X_2 is -NH-;

m is 1;

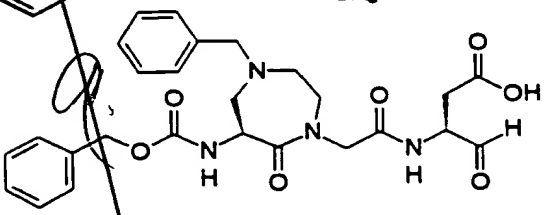
T is $-CO_2H$;

R_3 is $-CO-R_{13}$.

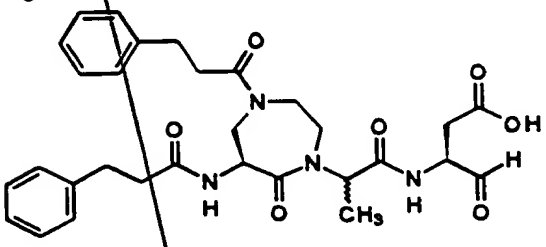
115. The compound according to claim 114, selected from the group consisting of:

114a 

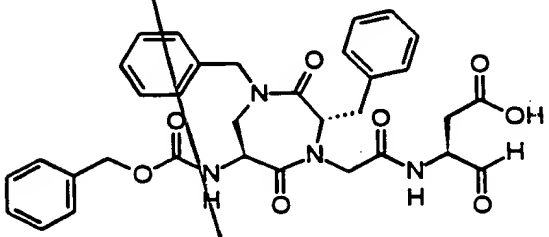
;

114b 

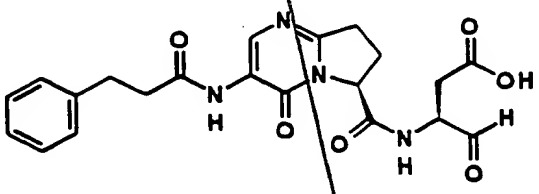
;

115 

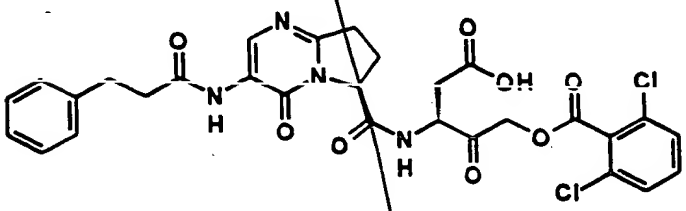
; and

121 

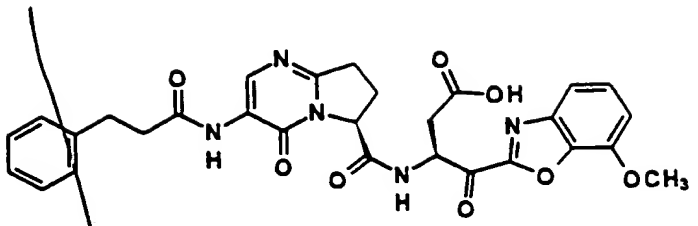
116. The compound according to claim 93, selected from the group consisting of:

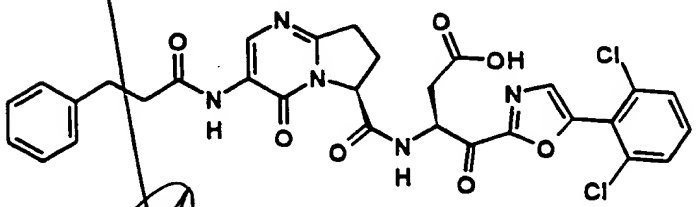
98 

;

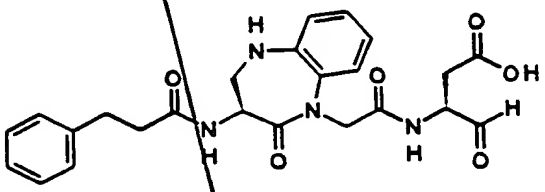
102a 

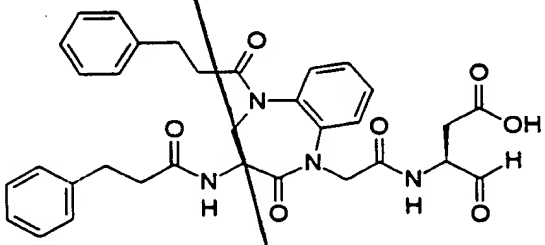
;

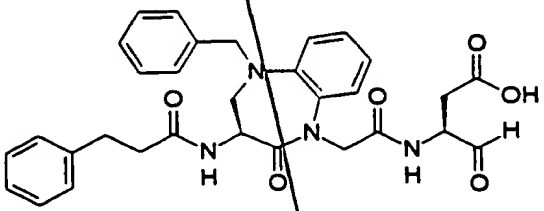
102b  ; and

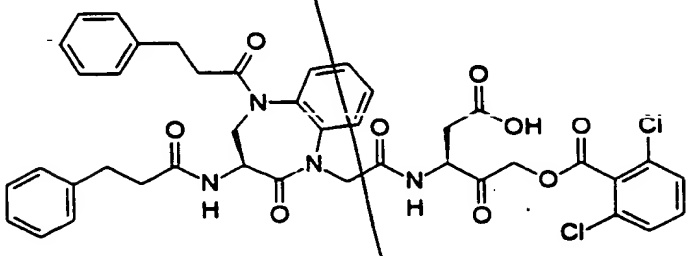
102c 

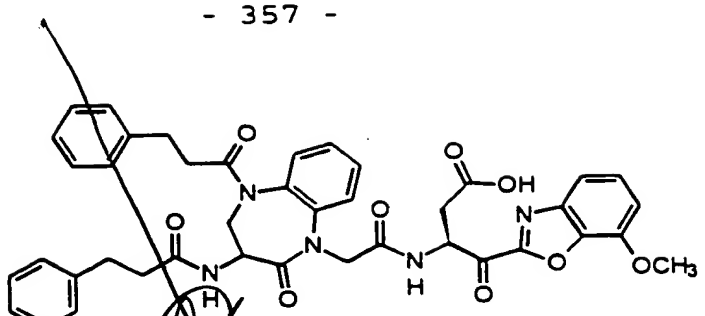
117. The compound according to claim 94, selected from the group consisting of:

106a  ;

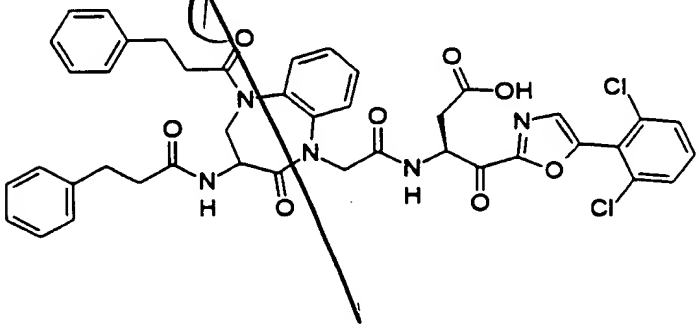
106b  ;

106c  ;

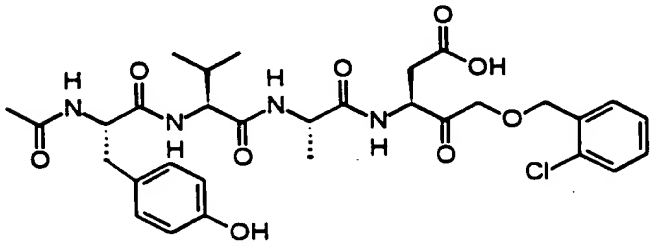
108a  ;

108b 

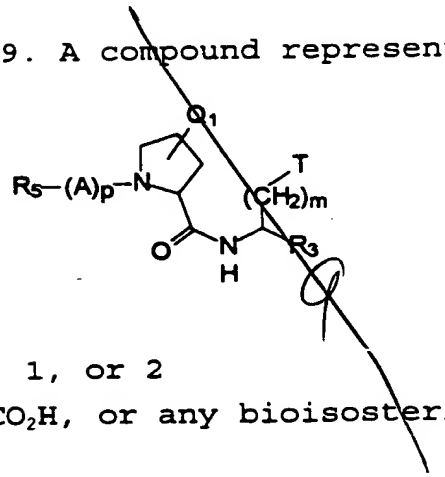
; and

108c 

118. The compound according to claim 105:

89 

119. A compound represented by the formula:



wherein:

m is 0, 1, or 2

T is $-CO_2H$, or any bioisosteric replacement for $-CO_2H$

R_3 is

-CN,

$-CO-R_{13}$, or

$-CO-CO-N(R_5)(R_{10})$;

R_5 is selected from the group consisting of:

-H,

$-Ar_1$,

$-CO-Ar_1$,

$-SO_2-Ar_1$,

$-R_9$,

$-CO-R_9$,

$-CO-O-R_9$,

$-SO_2-R_9$,

$-CO-N(Ar_1)(R_{10})$,

$-SO_2-N(Ar_1)(R_{10})$,

$-CO-N(R_9)(R_{10})$, and

$-SO_2-N(R_9)(R_{10})$;

each A is independently selected from the group consisting of any α-amino acid;

p is 2 or 3;

each R_9 is a C_{1-6} straight or branched alkyl group optionally singly or multiply substituted by -OH, -F,

or =O and optionally substituted with one Ar_1 group;

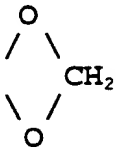
each T_1 is independently selected from the group consisting of:

-CH=CH-,
-O-,
-S-,
-SO-,
$-SO_2-$,
$-NR_{10}-$,
$-NR_{10}-CO-$,
-CO-,
-O-CO-,
-CO-O-,
$-CO-NR_{10}-$,
$-O-CO-NR_{10}-$,
$-NR_{10}-CO-O-$,
$-NR_{10}-CO-NR_{10}-$,
$-SO_2-NR_{10}-$,
$-NR_{10}-SO_2-$, and
$-NR_{10}-SO_2-NR_{10}-$;

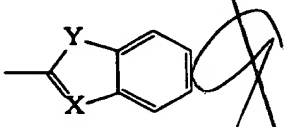
each R_{10} is independently selected from the group consisting of -H or a $-C_{1-6}$ straight or branched alkyl group;

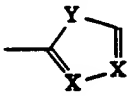
each R_{13} is independently selected from the group consisting of H, R_9, Ar_2, and $-CH_2-T_1-R_9$;

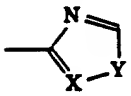
each Ar_1 is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings, a cycloalkyl group which contains between 3 and 15 carbon atoms and between 1 and 3

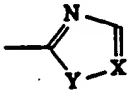
rings, said cycloalkyl group being optionally benzofused, and a heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocycle group containing at least one heteroatom group selected from -O-, -S-, -SO-, $-SO_2-$, =N-, and -NH-, said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by $-NH_2$, $-CO_2H$, -Cl, -F, -Br, -I, $-NO_2$, -CN, =O, -OH, -perfluoro C_{1-3} alkyl,  , or $-Q_1$; and

each Ar_2 is independently selected from the following group, in which any ring may optionally be singly or multiply substituted by $-Q_1$ and $-Q_2$:

(hh)  ;

(ii)  ;

(jj)  ; and

(kk)  ;

each Q_1 is independently selected from the group consisting of:

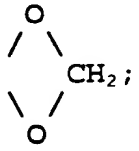
$-Ar_1$

$-O-Ar_1$

$-R_9$,

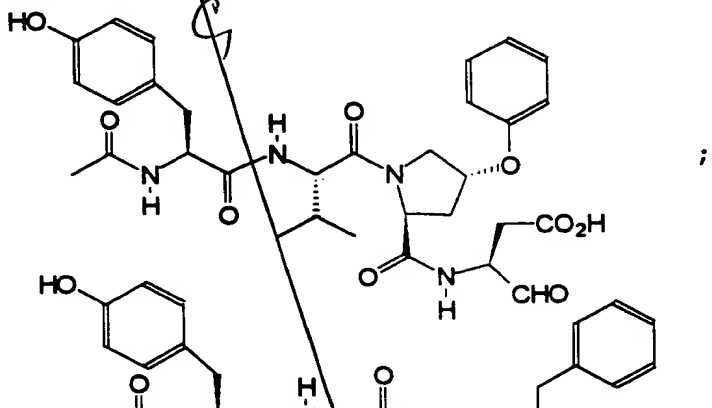
$-T_1-R_9$, and

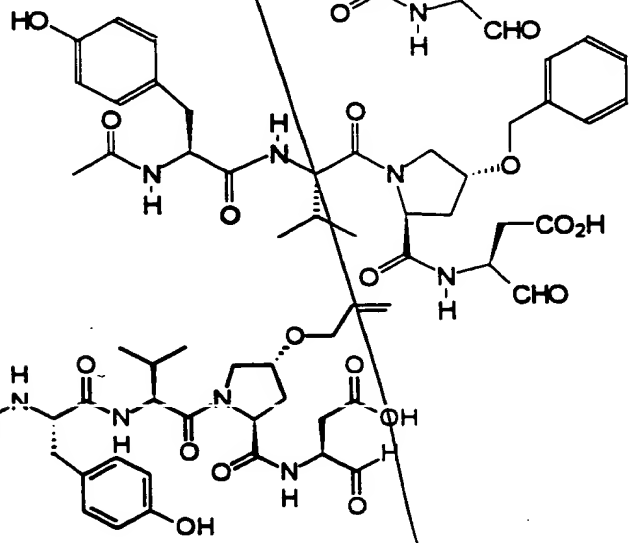
$-(CH_2)_{1,2,3}-T_1-R_9$;

each Q_2 is independently selected from the group consisting of -OH, $-NH_2$, $-CO_2H$, -Cl, -F, -Br, -I, $-NO_2$, -CN, $-CF_3$, and  ;

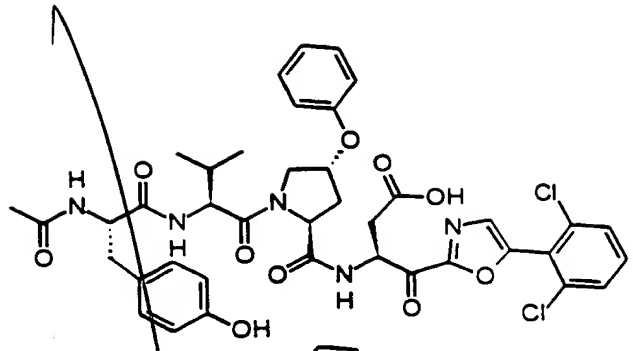
provided that when $-Ar_1$ is substituted with a Q_1 group which comprises one or more additional $-Ar_1$ groups, said additional $-Ar_1$ groups are not substituted with Q_1.

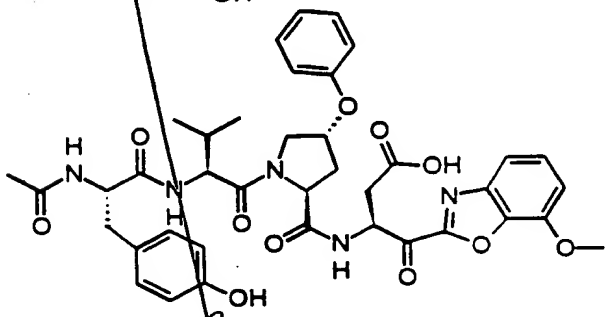
120. The compound according to claim 119, selected from the group consisting of:

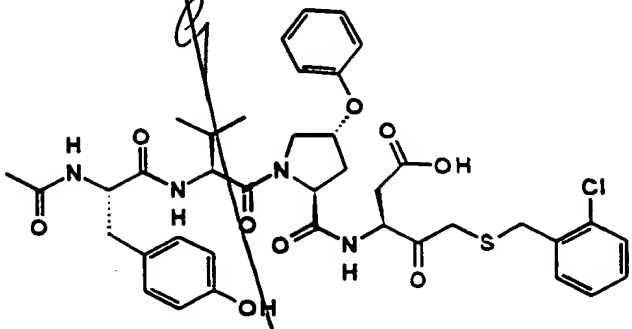
I  ;

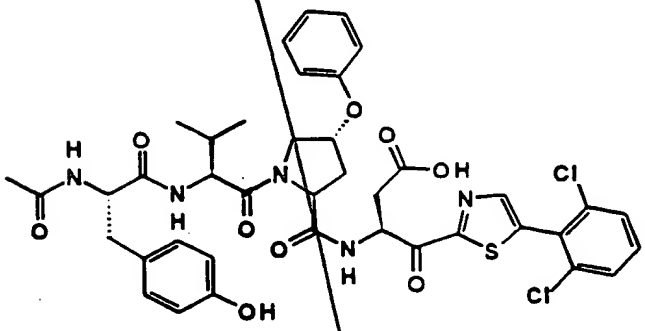
K  ;

;

156  ;

159  ;

161  ; and

162  .

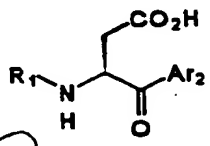
121. The compound acording to claim 119, wherein each A is independently selected from the group consisting of the α-amino acids:

alanine,

histidine,

lysine,
phenylalanine,
proline,
tyrosine,
valine,
leucine,
isoleucine,
glutamine,
methionine,
homoproline,
3-(2-thienyl) alanine, and
3-(3-thienyl) alanine.

122. A compound represented by the formula:



δ

R_1 is R_5-$(A)_p$-;

R_5 is selected from the group consisting of:
-H,
-Ar_1,
-CO-Ar_1,
-SO_2-Ar_1,
-R_9,
-CO-R_9,
-CO-O-R_9,
-SO_2-R_9,
-CO-N(Ar_1)(R_{10}),

$-SO_2-N(Ar_1)(R_{10})$,

$-CO-N(R_9)(R_{10})$, and

$-SO_2-N(R_9)(R_{10})$;

each A is independently selected from the group consisting of any α-amino acid;

p is 0, 1, 2, 3 or 4;

each R_9 is a C_{1-6} straight or branched alkyl group optionally singly or multiply substituted by -OH, -F, or =O and optionally substituted with one Ar_1 group;

each R_{10} is independently selected from the group consisting of -H or a C_{1-6} straight or branched alkyl group;

each T_1 is independently selected from the group consisting of:

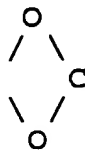
-CH=CH-,

-O-,

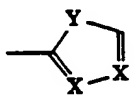
-S-,

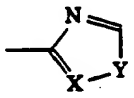
-SO-,

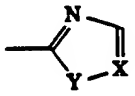
each Ar_1 is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings, a cycloalkyl group which contains between 3 and 15 carbon atoms and between 1 and 3

rings, said cycloalkyl group being optionally benzofused, and a heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocycle group containing at least one heteroatom group selected from -O-, -S-, -SO-, $-SO_2-$, =N-, and -NH-, said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by $-NH_2$, $-CO_2H$, -Cl, -F, -Br, -I, $-NO_2$, -CN, =O, -OH, -perfluoro C_{1-3} alkyl,  , or $-Q_1$; and

each Ar_2 is independently selected from the following group, in which any ring may optionally be singly or multiply substituted by $-Q_1$ and $-Q_2$:

(ii)  ;

(jj)  ; and

(kk)  ;

each Q_1 is independently selected from the group consisting of:

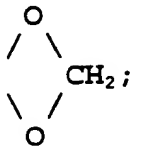
$-Ar_1$

$-O-Ar_1$

$-R_9$,

$-T_1-R_9$, and

$-(CH_2)_{1,2,3}-T_1-R_9$;

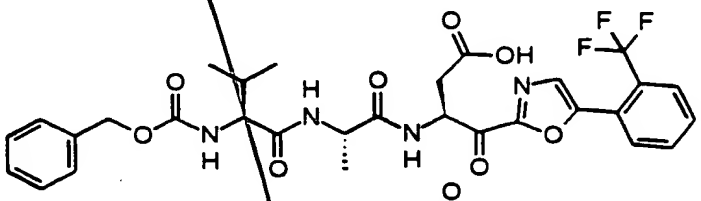
each Q_2 is independently selected from the group consisting of -OH, $-NH_2$, $-CO_2H$, -Cl, -F, -Br, -I, $-NO_2$, -CN, $-CF_3$, and  ;

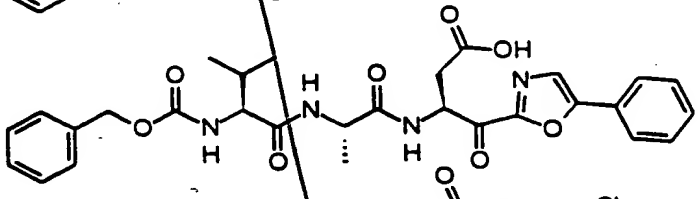
provided that when $-Ar_1$ is substituted with a Q_1 group which comprises one or more additional $-Ar_1$ groups, said additional $-Ar_1$ groups are not substituted with Q_1;

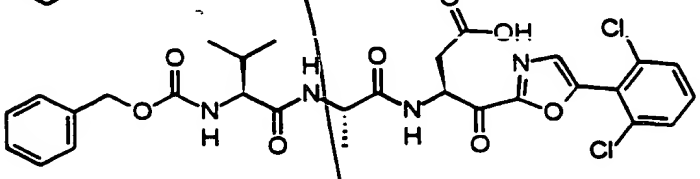
each X is independently selected from the group consisting of =N-, and =CH-; and

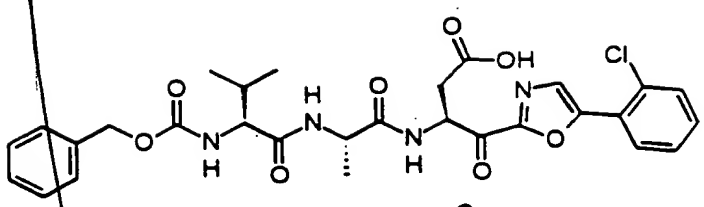
each Y is independently selected from the group consisting of -O-, -S-, and -NH.

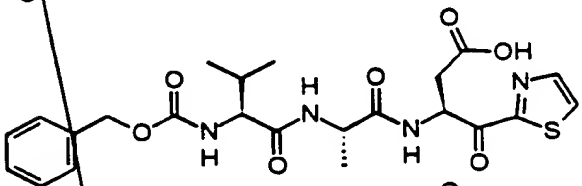
123. The compound according to claim 122, selected from the group consisting of:

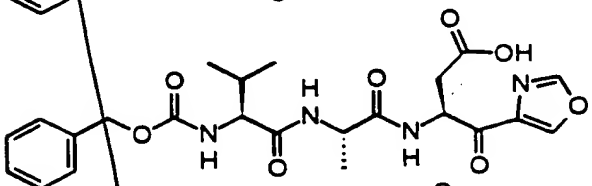
144  ;

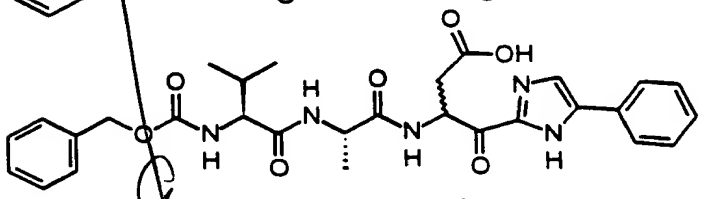
145  ;

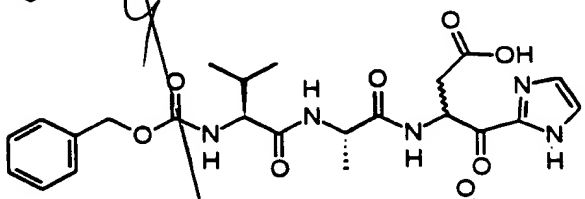
146  ;

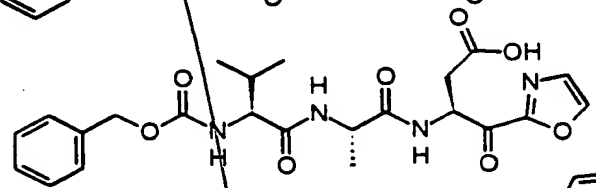
147  ;

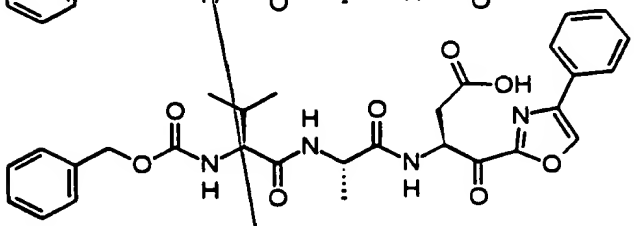
148  ;

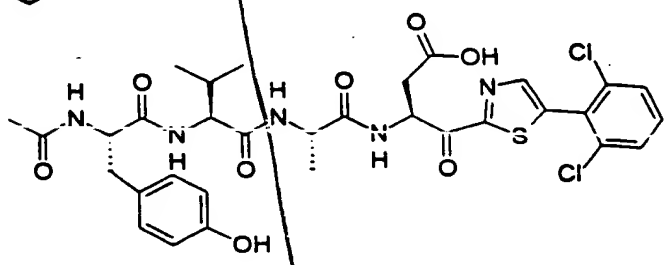
149  ;

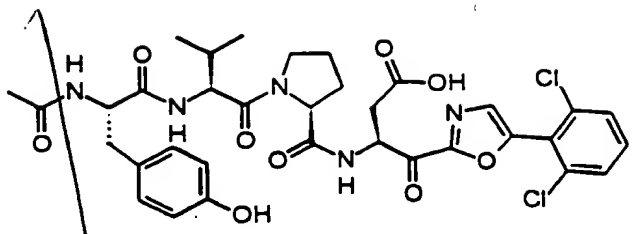
150  ;

151  ;

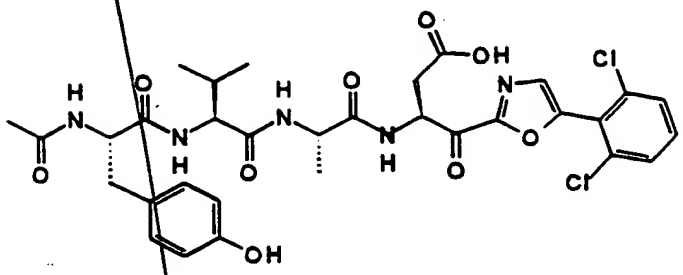
152  ;

153  ;

154  ;

155 

; and

163 

124. The compound according to claim 122, wherein each A is independently selected from the group consisting of the α-amino acids:

alanine,
histidine,
lysine,
phenylalanine,
proline,
tyrosine,
valine,
leucine,
isoleucine,
glutamine,
methionine,
homoproline,
3-(2-thienyl) alanine, and
3-(3-thienyl) alanine.

Add a2